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Monthly Message

The Services have received many inquiries as to what effect Public Law 497 has had upon the number of resignations of medical and dental officers and also as to increase in the number of Regular officers. This Act, known as the Medical and Dental Officer Career Incentive Act, became effective on 1 May 1956. Colonel Charles H. Gingles, MC, USA, has just compiled the following table from statistics presented to him by the Army, Navy, and Air Force.

TABLE 1. *Resignations from the Regular Medical and Dental Corps in the entire Department of Defense during fiscal years 1954 to 1958 as compared to average strength during those years*

Fiscal year	Medical Corps			Dental Corps		
	Average strength	Resignations		Average strength	Resignations	
	Number	Number	Per cent	Number	Number	Per cent
1954	2777	446	16.1	1447	110	7.6
1955	3342	363	10.9	1380	76	5.5
1956	3316	193	5.8	1436	22	1.5
1957	3613	114	3.2	1605	13	0.8
1958 (July to Nov.)	4006	52	1.3	1747	9	0.5

Part of the high resignation rate in FY 1954 and 1955 was due to "pent-up" resignations. It is particularly interesting to note, however, that beginning with FY 1957 resignations have been running at a very low rate.

It will be noticed that during the same period the 12-month average strength in all three services has steadily increased. Again part of this increase may be due to those who are in the various residency training programs. So far, however, about 70 per cent of those in these programs have signified their intention of remaining in the Regular Service, although it is too early to draw a definite conclusion.

Frank B. Berry

FRANK B. BERRY, M. D.
Assistant Secretary of Defense
(Health and Medical)

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Foreword

The *United States Armed Forces Medical Journal* is the medium for disseminating information of administrative and professional interest to all medical personnel of the Department of Defense. The Assistant Secretary of Defense (Health and Medical) and the Surgeons General of the several services invite all medical officers, dental officers, Medical Service Corps officers, Nurse Corps officers, and officers of the Veterinary Corps of the Armed Forces, and the medical consultants of the Army, Navy, and Air Force to submit manuscripts for publication in this *Journal.*

FRANK B. BERRY, M. D.,
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UNITED STATES ARMED FORCES
MEDICAL JOURNAL

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ACUTE RADIATION SYNDROME IN MAN

Military and Civil Defense Aspects

HERBERT B. GERSTNER, *M. D.*

IN AN ADDRESS to the 62d Annual Convention of the Association of Military Surgeons of the United States held in November 1955, Major General James P. Cooney, Deputy Surgeon General of the Army, stated:

> In the past ten years a great deal of effort has been spent in trying to understand and teach various detailed effects of nuclear weapons. Some of the effort has involved discussions of detailed physics and mathematics relating to the bomb and the microseconds following the detonation. This approach has led to a preoccupation with details that will not help us as medical people to solve the casualty problems. In addition, the preoccupation with these details has resulted in the creation of an aura of mystery around the weapon that has prevented the average individual from understanding the things that are essential to him and to his neighbor if they are to survive.[1]

Now that nuclear energy is already producing electricity, propelling ships, and forming the basis for devastating weapons, and now that long-range ballistic missiles capable of carrying nuclear warheads can be assumed to exist, everybody concerned with practical medicine is compelled to acquaint himself with effects of ionizing radiation on man. Widespread ignorance of these effects may be attributed to the fact that presently known parts of the data are too widely dispersed over numerous professional journals, or hidden in practically inaccessible documents, to allow easy composition of a comprehensive picture; also, the

From Department of Radiobiology, Air University School of Aviation Medicine, USAF, Randolph Air Force Base, Tex. Report 58-6 of November 1957.

factual evidence is frequently clouded by emotional and political considerations. Under these circumstances it is difficult to arrive at an objective and sensible judgment.

The present report, restricted to the acute effects of human whole-body exposure to penetrating ionizing radiation, attempts a realistic evaluation of facts as they are known at this time. Clinical features essential from the standpoint of the practical physician and the medical officer have been emphasized, while those of more academic interest have been omitted or treated cursorily. Such an endeavor to present to the practitioner a coherent and unified clinicopathologic concept on which to base his actions, necessarily must involve oversimplifications that, with increasing information, may be subject to revision.

In case of accidental or intentional nuclear explosions, an estimate can be made of the air dose of penetrating ionizing radiation to which a group of persons has been exposed. The physician then called into action will face two questions of paramount importance: (1) Is it possible, from the air dose, to predict the fate of the exposed persons—that is, to arrive at a reasonably correct prognosis? (2) Is it conceivable, from the air dose, to anticipate for a population the degree and the time course of the ensuing disease, and thereby to estimate the medical requirements—personnel, hospital beds, and supplies?

THE "TYPICAL" ACUTE RADIATION SYNDROME

Exposure to a sufficient amount of penetrating x-ray, gamma, or neutron radiation causes in man characteristic clinical sequelae—the acute radiation syndrome. This complex of signs and symptoms, unfolding along a rather fixed time schedule, forms a peculiar picture that is as well defined as "lobar pneumonia" or "typhoid."

The most conspicuous features of the "typical" radiation-induced disease are as follows: Within 2 hours after exposure, complaints pointing to an "upset stomach" develop rather abruptly; anorexia, nausea, and malaise are predominant and are accompanied by listlessness, drowsiness, and fatigue. Deterioration of the individual's general condition progresses rapidly and leads to profuse vomiting, extreme weakness, or even prostration. This early reaction culminates about 8 hours after exposure and then subsides rather quickly. On the 2d postradiation day, nausea and occasional vomiting persist but the general condition is markedly improved; on the 3d postradiation day all complaints have disappeared. To avoid confusion, the burst of early signs and symptoms should not be designated as "radiation sickness" but rather as "initial reaction" or as the "prodromal phase" of the acute radiation syndrome. After dissipation of prodromal effects, the patient is asymptomatic and capable of performing normal work,

or even of exerting strenuous physical effort. This favorable state, the "latent period," may extend to the 19th or 20th post-radiation day, when a new phase is entered rather abruptly. As in the acute onset of an infectious disease, the patient experiences chills, malaise, a feverish feeling, fatigue, and shortness of breath on exertion. Again the general condition deteriorates rapidly and, within 2 or 3 days, hospitalization becomes necessary. Manifestations of severe bone marrow depression—characterized hematologically by leukopenia, thrombocytopenia, and anemia—appear in the form of frank hemorrhages, purpura, susceptibility to infection (especially in the oral cavity), fever, and other signs and symptoms associated with such disorders of the blood picture. This phase of aplastic anemia culminates about the 30th day when the patient passes through a critical state. Thereafter recovery starts and becomes obvious between the 40th and 50th days; when fever disappears, infectious lesions in the oral cavity heal, and the blood picture approaches normal values. Convalescence begins after the 60th day and is followed by resumption of work and normal life approximately 3 months postexposure.

According to their chronologic sequence, four distinct stages of the acute radiation syndrome can thus be established—namely, prodromal, latent, bone marrow depression or aplastic anemia, and recovery phases (fig. 1).[2] Of course, the "typical" disease, as described above, will be subject to variation and modification brought about essentially by two factors—dose and individual susceptibility. Before these modifications can be discussed, however, a survey must be made of the material on which the analysis is based.

ORIGIN OF DATA USED FOR EVALUATION

The largest group of persons exposed to nuclear radiation is represented by the populations of Hiroshima and Nagasaki. Careful and comprehensive clinical[2,3] as well as pathologic[3,4] observations are available. Although these data are outstanding for establishing consequences of human exposure to ionizing radiation, they are of rather limited value for deriving dose-effect relationships, since frequently even a rough estimate of the dose is impossible. Subsequently, reference to the Japanese bomb casualties appears under the abbreviation *JBC*. On 1 March 1954, the test explosion of a hydrogen device at Bikini Atoll accidentally exposed 28 Americans and 239 Marshallese to fallout radiation. Determinations of dose and clinical sequelae are well documented.[5-7] According to the four islands on which these persons were located, four dose groups can be formed that will subsequently be designated as MI_1 (Utirik), MI_2 (Ailinginae), MI_3 (Rongerik), and MI_4 (Rongelap Atoll). During the same test shot, 23 Japanese

aboard a fishing boat were also exposed to fallout radiation. This group, for which dose and clinical sequelae are relatively well known,[8-10] will subsequently be designated as *JF*.

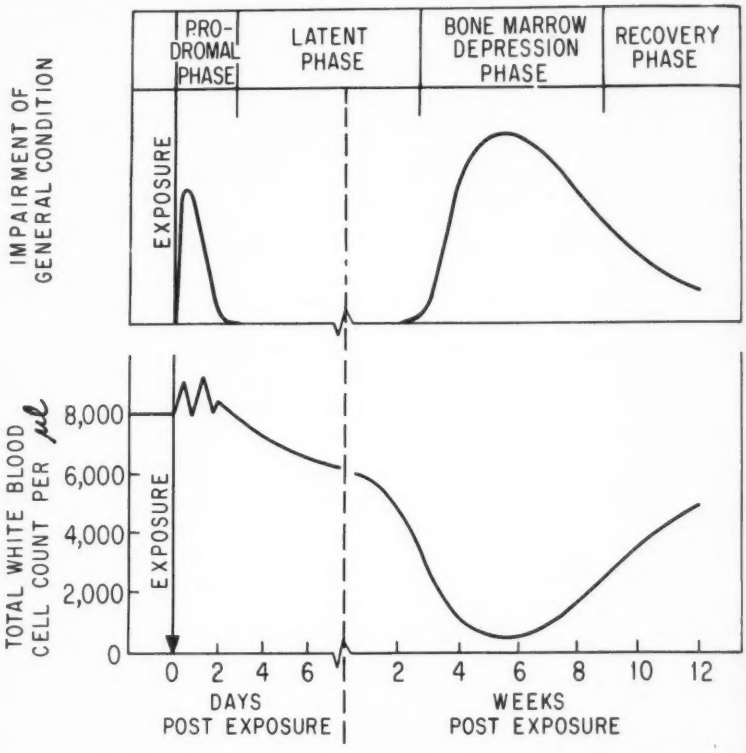

Figure 1. Schematic drawing showing the typical clinical course of the acute radiation syndrome (hematopoietic form). The platelet count would parallel the white blood cell count while lymphocyte count would decline earlier and recover later.

Two nuclear accidents occurred at the Los Alamos Scientific Laboratory. Uncontrolled fission reactions caused the inadvertent exposure of 10 persons to complex ionizing radiation. Detailed analysis of dose[11] and clinical course[12] are available for 9 of these cases. They will be designated as $LA_1 \ldots LA_{10}$, keeping the indices identical with Hempelmann's numbering of the patients. On 2 June 1952, at the Argonne National Laboratory, 4 persons were exposed to neutron and gamma radiations released by the accidental excursion of a water-moderated critical assembly. Doses and clinical pictures have been well established for each individual patient.[13] These cases will be designated as A_1, A_2, A_3, and A_4. At the Geneva Conference on Peaceful Uses

of Atomic Energy, Guskova et al.[14] reported 2 Russian cases of the acute radiation syndrome as the result of a short gamma and neutron irradiation, after the rules of operating an experimental reactor had been violated. These 2 patients, for whom dose and clinical course are well reported, will be designated as R_1 and R_2.

Over a long period of time, through radiotherapy, a wealth of information about effects of ionizing radiation on man has accumulated. By definition, however, the treatment of the patient will be such that generally only local reactions occur and severe systemic responses will be avoided. In several instances, nevertheless, relatively high doses of whole-body x-irradiation have been administered as a palliative procedure in advanced and generalized neoplastic disease. European experience with this type of treatment, termed *teleroentgen therapy,* was summarized in an optimistic report given by Mallet at the International Cancer Congress at Brussels in 1936. Later publications[15] were more reserved and warned of serious complications that might be encountered in the higher dose range. An interesting method of whole-body exposure was developed by Heublein.[16] Several patients, lying in their beds, received simultaneously irradiation from a strongly filtered x-ray unit at a distance of 5 meters. Exposure lasted through 20 hours of each day and was continued until doses up to 300 r had been accumulated; during 1 week approximately 100 r were delivered. Medinger and Craver[17] reported on 270 patients treated by this technic. To answer some medical questions that arose in connection with the Manhattan Project, the effect of whole-body exposure to x-rays was studied in several groups of patients undergoing radiotherapy and in one group of 3 healthy volunteers.[18–20] Following introduction of chemotherapy as a palliative procedure in advanced cancer patients, whole-body x-irradiation was re-examined and its effectiveness compared with that of various cancerocidal substances.[21, 22] Unfortunately, the above-listed clinical material is of limited value for the present analysis since, predominantly, radiotherapeutic effects have been well described, while systemic reactions as related to dose have only occasionally been mentioned. Therefore, these clinical groups together will subsequently be considered as a whole. Recently, a detailed study—comprising dosimetry,[23] radiobiologic aspects,[24] and therapeutic evaluation[25]—has been reported on 263 cancer patients. These data will subsequently be designated as *MDA*.

Singly, each of the above-listed sources—bomb casualties, accidental exposures, and radiotherapeutic irradiation—are inconclusive because they are compromised by the facts that either the dose and type of irradiation are ill-defined (*JBC*), or that whole-body exposure to penetrating rays is complicated by simul-

taneous superficial effects of alpha and beta radiation (*MI* and *JF*), or that the exposed person is not a healthy human being (*MDA*). Collectively, however, these data allow reasonable conclusions about the interrelationship between dose and clinical course, as shown in the following section.

DEPENDENCY OF THE ACUTE RADIATION SYNDROME ON AIR DOSE

Analysis of the relationship between dose and clinical effect first requires definition of the two terms. The *air dose*, to which a certain person has been exposed, is exactly known only in cases of therapeutic application where quality and quantity of ionizing radiation can readily be measured. In all other instances these factors have been derived by estimation, frequently a very difficult problem because of the complex nature of the radiation —ranging through a wide section of the electromagnetic spectrum, and containing various amounts of corpuscular components. In these cases, therefore, designation of the air dose in roentgens is subject to a considerable margin of error; however, since a similar degree of uncertainty may exist in future emergency situations, such a crude procedure appears justified. A detailed discussion of the dosimetry problem lies beyond the scope of this report. The severity of radiation-induced clinical sequelae will subsequently be designated as *trivial, light, moderate, serious, grave,* and *lethal: Trivial* denotes subtle and very transitory deviations from normal, or none at all; *light*, mild signs and symptoms requiring neither medical attention nor treatment; *moderate,* well-developed radiation syndrome manageable ambulatorily; *serious,* hospitalization necessary, good chance for recovery; *grave,* poor chance for recovery; *lethal,* no chance for recovery. In the following paragraphs the clinical effects will be discussed as they develop with increasing air dose (tables 1 and 2).

Dose range: 0-50 r

As shown by the corresponding section of table 1, this dose range is generally asymptomatic and, without exception, the clinical course is trivial. Case A_4, on the 15th day after exposure, displayed in the right eye, immediately inferior to the limbus of the optic disk, a very small, flame-shaped hemorrhage (*a* in table 1) that disappeared one month later. The MI_1 group showed indications of a slight depression of leukocytopoiesis (*b*) since lymphocyte and thrombocyte counts were somewhat lower than those of the controls, especially around the 29th postexposure day when the maximal effect on the peripheral blood elements must be expected to occur. Case LA_9 felt nauseated (*c* in table 1) several hours after the accident but ascribed this symptom to nervousness and apprehension. Among the *MDA* cases only one patient reported a brief episode of nausea on the day of treatment,

TABLE 1. *Dependency of the acute radiation syndrome on air dose, subthreshold range*

TABLE 1. *Dependency of the acute radiation syndrome on air dose, subthreshold range*

Source of information	Number of cases	Air dose (r)	Prodromal phase	Bone marrow depression	Frank hemorrhage	Purpura	Infection	Fever	Epilation	Diarrhea	Clinical course*
Dose range, 0 – 50 r											
A_4	1	12	–	–	a	–	–	–	–	–	T
MI_1	157	14	–	b	–	–	–	–	–	–	T
LA_2	1	31	–	–	–	–	–	–	–	–	T
LA_{10}	1	35	–	–	–	–	–	–	–	–	T
LA_9	1	45	c	–	–	–	–	–	–	–	T
MDA	188	15-50	–	–	–	–	–	–	–	–	T
Dose range, 51 - 100 r											
LA_8	1	60	–	d	–	–	–	–	–	–	T
MI_2	18	69	e	f	–	–	g	h	i	–	T
A_3	1	70	j	–	–	–	–	–	–	–	T
MI_3	28	78	–	k	–	–	–	–	–	–	T
MDA	26	75-100	–	–	–	–	–	–	–	–	T
Dose range, 101 - 150 r											
LA_7	1	145	–	–	–	–	–	–	–	–	T
MDA	13	125-150	l	m	–	–	–	–	–	–	T, L, M

*T - Trivial.
L - Light.
M - Moderate.
Lower case letters are explained in text.

TABLE 2. *Dependency of the acute radiation syndrome on air dose, subthreshold range*

Source of information	Number of cases	Air dose (r)	Prodromal phase	Bone marrow depression	Frank hemorrhage	Purpura	Infection	Fever	Epilation	Diarrhea	Clinical course*
Dose range, 151-200 r											
A_2	1	160	–	+	–	–	–	–	–	–	T
MI_4	64	175	+	+	–	–	n	o	p	–	T,L,M
A_1	1	190	+	+	–	–	–	–	–	–	M
LA_6	1	197	–	–	–	–	–	–	–	–	T
MDA	36	175-200	+	+	+	q	r	s	–	–	L,M,S
Dose range, 201-400 r											
R_1	1	300	+	+	+	+	t	+	+	–	S
JF	23	200-400	+	+	+	+	+	+	+	–	M,S,G
Dose range, 401-600 r											
LA_4	1	416	+	+	+	–	–	+	+	–	S
R_2	1	450	+	+	+	+	+	+	–	–	G
LA_1	1	590	+	+	+	–	+	+	+	+	Lethal

*T - Trivial.
L - Light.
M - Moderate.
S - Serious.
G - Grave.
Lower case letters are explained in text.

while the rest were completely asymptomatic. In connection with the Manhattan Project, 3 healthy volunteers received 21 r of x-radiation to the whole body; they showed neither hematologic changes nor any other adverse effect.[18] The same was true in a group of cancer patients, with the exception of a slight decline in lymphocytes occurring rather consistently at doses of 40 r or higher.[19] *In summary, then, it can be stated that the dose range from 0 to 50 r is subthreshold for the acute radiation syndrome and presents no medical problem in emergency situations.* From a purely military standpoint, a recent British publication[26] concludes that at this level no serious disability is to be expected and that the irradiation can be ignored, apart from recording its occurrence.

Although a thorough discussion of possible late effects and genetic consequences of exposure to ionizing radiation does not belong to the objectives of the present report, a few remarks appear appropriate at this time. All evidence, supplied by thousands of patients having received therapeutic doses in this range and by bomb and accident data so far as they can be evaluated today, points to the fact that acute reactions, if existing at all, will completely disappear and that perfect recovery will occur. Shields Warren, in the foreword to reference 12, states: "The story of the survivors shows that an individual can be exposed to a large dose of radiation and still return to a productive vigorous life." The concepts of accelerated aging and shortening of life span,[27] as dervied from contradictory animal experiments, should not be applied to man, at least not in the low dose ranges, until they can be founded on strong affirmative observations. Tolerance to additional small amounts of irradiation will practically be normal. In this respect the National Committee on Radiation Protection and Measurement[28] declares: "An accidental or emergency dose of 25 rems (roentgen equivalent man) to the whole body, occurring only once in the lifetime of the person, shall be assumed to have no effect on the radiation tolerance status of that person." At the Chalk River Conference (quoted from reference 29) it was agreed that no manifest permanent injury is to be expected for a single exposure of the whole body equivalent to 25 r or less, with a possible exception in the case of pregnant women. Evidently, as far as the exposed individual is concerned, doses up to 50 r do not present clinical problems; however, they may assume significance for future generations if large numbers of the younger population have been irradiated. Animal experiments suggest that doses of 30 to 50 r will probably double the spontaneous mutation rate in man. Since most of the mutations are undesirable, this increased rate may be a real problem for the nation as a whole. However, much more information is required before the size of the potential genetic hazard can be realistically assessed.

Dose range: 51-100 r

As revealed by the corresponding section of table 1, this dose range is subthreshold for the acute radiation syndrome, and the clinical sequelae are consistently trivial; however, a few sporadic individuals with high radiosensitivity show indications of a beginning, though clinically insignificant, depression of leukocytopoiesis: between the 3d and 6th week the lymphocyte count is well below normal, while the granulocytes decrease to slightly subnormal values. In case LA_8 the total leukocyte count had fluctuated between 5,500 and 8,000 cells per cubic millimeter prior to the accident; after exposure it showed a typical initial period of instability (fig. 1) and then declined gradually to a minimum of 5,000 around the 20th day (*d* in table 1). Among the MI_2 population, only one member showed mild prodromal symptoms with nausea (*e*) during the first 2 days postexposure. The group means for white blood cells, neutrophils, and lymphocytes appeared to be slightly subnormal (*f*) throughout several months, while the platelets showed a definite minimum between the 20th and 30th postradiation days. From a clinical standpoint, however, these changes were inconspicuous, the maximal depression of the total white count being somewhat below 5,000 in 3 cases only. Between the 27th and 42d postexposure days there occurred an epidemic of upper respiratory diseases (*g, h*) which most likely was unrelated to irradiation. Epilation and skin injuries (*i*) definitely were consequences of direct contact with fallout material. On the 3d postradiation day case A_3 vomited on several occasions (*j*) and had four loose stools. These effects were believed to be manifestations of anxiety and tension rather than reflections of a true prodromal phase. Findings in the MI_3 group (*k*) essentially paralleled those of the MI_2 population; however, there was no case with prodromal symptoms, and neither epilation nor skin lesions developed because of early decontamination. The 26 patients of the *MDA* series as well as 4 additional cases exposed to 60 r[18] were completely asymptomatic with the exception of a slight decrease in lymphocytes occurring in the latter cases. *In summary, then, it can be stated that doses between 51 and 100 r will cause, if at all, but trivial and transitory clinical changes posing no medical problem.* According to present-day knowledge these mild acute effects are followed by complete recovery and return to normal life. Nevertheless, additional irradiation should be restricted as much as possible since a lowering of radiation tolerance may persist. As to this dose range a British publication[26] concludes approximately as follows: Slight, but not incapacitating, illness may occur in a number of cases. There is no need to break off an important military mission; however, as soon as convenient, the exposed men should be placed under medical observation for 60 days, and symptoms should be treated as they

arise. Afterwards, for about one-half year, monthly blood counts should be performed.

Dose range: 101-150 r

Although, as shown by the corresponding section of table 1, observations are too few to allow a definite statement, the *MDA* data suggest the following: The acute radiation syndrome, with well-developed prodromal and bone marrow depression phases, becomes noticeable in about one third of the exposed persons (*l, m*). Consistently, however, these changes are so moderate in degree that they can be handled ambulatorily and, therefore, do not pose clinical problems. Three additional patients exposed to 120 r remained asymptomatic.[18] *Hence, conclusions parallel those given for the previous dose range.*

Dose range: 151-200 r

This most important range is well documented as revealed by the corresponding section in table 2. Dose and clinical course have been established for two relatively large groups—MI_4 and *MDA*. Since these data represent the best ones known for man, some detailed discussion appears appropriate. The typical acute radiation syndrome, evolving in its four phases along a rather fixed time schedule (fig. 1), was clearly noticeable in approximately 70 per cent of the MI_4 group and in 90 per cent of the *MDA* patients.

Among the MI_4 population, about two thirds experienced nausea and one tenth reported vomiting and loose stools. Without therapy these effects had subsided by the 3d postradiation day. The bone marrow depression phase varied in degree from trivial to moderate. In all of the exposed persons both platelet count and total white blood cell count decreased and were at a minimum between the 25th to the 30th and between the 40th to the 45th day, respectively. More revealing, from a clinical standpoint, are the following findings: Of the entire population 10 per cent reached platelet values of less than 65,000; 50 per cent attained a white blood cell count of less than 4,000; and 10 per cent fell to a white blood cell count of less than 1,500 per μl. However, even the patients showing the most pronounced depression must still be considered as border line between moderate and serious since they did not develop definite clinical complications and remained physically active; frank hemorrhages and purpura were absent; blood transfusion was not required. The epidemic of upper respiratory diseases that spread through the Marshall Islands between the 27th and 42d postexposure days (*n, o*) caused, in the group with low leukocyte counts, neither greater incidence nor clinical signs and symptoms of greater severity than in the other groups. Therefore, in agreement with radiotherapeutic experience, Cronkite et al.[7]

concluded that such degrees of radiation-induced bone marrow depression are still well tolerated, and that coincidence between epidemic and height of radiation effects was caused probably by chance. Again, epilation and skin injuries (*p*) definitely were consequences of direct contact with fallout material.

Among the *MDA* patients 15 per cent remained asymptomatic during the prodromal phase, while 35 per cent experienced nausea alone, and 50 per cent reported nausea with vomiting. In the majority of instances, these complaints could be handled by psychologic reassurance; however, 5 cases required additional medication of chlorpromazine hydrochloride, and 2 patients were so severely affected as to demand parenteral fluid supply. On the 3d postradiation day the initial reactions had subsided. After a latent period of about 3 weeks, the patients entered the bone marrow depression phase, ranging in severity from trivial to serious. In a group of 20 patients who could be observed regularly, all developed thrombocytopenia with a platelet count of less than 70,000 per μl, reaching the minimum on the 25th day; 8 exhibited leukopenia with fewer than 2,500 white cells per μl, the group mean passing through a minimum on the 32d day; and 2 displayed a white blood cell count of fewer than 1,000 per μl. During the bone marrow depression phase, complications were as follows: frank hemorrhage was common; it was mostly self-limited, however, and of little clinical concern; purpura occurred in 4 patients (*q*); and infection developed in 1 case (*r, s*). The clinical course of the acute radiation syndrome must be classified as serious in at least 3 of the patients. Here, hospitalization and intensive medical treatment with repeated blood transfusions and antibiotics were mandatory.

Under the assumption that air dose specifications for the *MI*, and *MDA* groups are comparable (analysis of the problem lies beyond the scope of the present report) and under the assumption that tolerance to penetrating ionizing radiation is not materially different between healthy human beings and advanced cancer patients, the following summarizing statements can be made: *In the dose range from 150 to 200 r the acute radiation syndrome becomes noticeable in the majority of an exposed population, and it reaches clinical significance in a few highly radiosensitive persons. Approximately 200 r will be the clinical tolerance dose, or the threshold dose, beyond which an appreciable number of individuals among the exposed population can be expected to develop significant complications requiring hospitalization and intensive medical treatment.* The preceding statement is also supported by additional radiotherapeutic experience[16, 17, 21, 22] indicating that whole-body doses up to 200 r are relatively "safe," whereas serious complications may occur at higher dose levels.

Present-day knowledge leads to the conclusion that in this dose range, complete recovery will follow after the patient passes through the acute radiation syndrome, even in its more severe forms. Physical fitness and work capacity, when impaired, will have returned to normal values about 3 to 4 months following exposure, while complete restoration of the blood picture may frequently require a much longer period of time (*MI* groups and *JBC*). It is evident that additional irradiation should be kept as low as possible because of a decreased tolerance level.

Dose range: 201-400 r

In this dose range, as revealed by the corresponding section of table 2, the acute radiation syndrome is fully developed and ranges in severity from moderate to grave. Case R_1 displayed the disease almost in its classical form. A 3-day prodromal phase with general weakness, headache, drowsiness, nausea, and vomiting was followed by a latent phase extending through more than 2 weeks. Abruptly on the 24th postexposure day, the bone marrow depression phase became evident clinically by pronounced general debility, insomnia, fever, petechial bleeding into the skin, frank hemorrhage from the gums, and a drop in white blood cell count, reaching a minimum of 780 per μl, at about the 33d day. Infection was absent (t) probably because of the early prophylactic administration of antibiotics. Entrance into the recovery phase became conspicuous during the 7th postexposure week. Complete restoration of health and work capacity ensued, as judged by a final medical examination at 1½ years after the accident.

Discussion of the *JF* group seems justified since, here, several important aspects of the acute radiation syndrome are well demonstrated. Early in the morning of 1 March 1954, while the fishermen (17 to 39 years of age) were laying out their nets about 100 miles off Bikini, they saw a faint red light on the westerly horizon, and 7 minutes later they heard a dull noise followed by two sharp explosionlike sounds. Three hours thereafter fleecy clouds appeared, and a white substance began to descend from the sky. This fallout continued for 5 hours, and the deck of the boat looked as if it was covered by frost. Within a few hours the crew complained of fatigue, headache, drowsiness, loss of appetite, nausea, and vomiting; they felt so tired that they slept almost continuously except when aroused by other members. All reactions were relatively mild, however, and had completely disappeared by the 4th day. With the exception of minor skin lesions, obviously caused by direct contact with fallout material, the crew was asymptomatic and in good spirits during the entire return voyage that lasted 13 days. On arrival in Japan, 2 men had skin injuries serious enough to require hospitalization; the others went home or remained on the boat. They looked healthy and felt quite well. Within 2 weeks

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(4 weeks after start of exposure) however, the entire crew and the captain had to be hospitalized because of signs of a progressing bone marrow depression. Fatigue, fever, and infection were common, while hemorrhagic diathesis was occasional. Total white blood cell and thrombocyte counts were at the minimum between the 30th and 45th days. At the time of severest depression, the white blood cell count fell below 4,000 in all crew members, below 3,000 in 18, below 2,000 in 5, and to 1,000 or less in 2 men. Throughout April, 4 to 8 weeks after start of exposure, the general clinical condition of the fishermen remained serious; then improvement became evident. In the majority of cases, the blood picture returned to normal rather quickly; however, in several instances recovery proceeded slowly and encompassed a period of several months. The acute radiation syndrome was complicated by acute hepatitis that appeared in 17 of the 23 fishermen during the middle of May, and caused 1 man's death on 23 September 1954, almost 7 months after exposure. That hepatitis had previously caused the death of 2 brothers of the deceased is noteworthy. Although the etiology of this burst of hepatitis in the fishermen remains unsolved, the following possibilities are listed in declining order of probability: first, serum hepatitis induced by numerous blood transfusions; second, hepatitis promoted by decreased resistance to infection; and third, hepatitis due to internal contamination with fission products. Since the fallout material was not evenly distributed over the boat, and since the shielding effect of the ship's structures varied at different locations, the crew had been exposed to gamma doses probably ranging from 200 to 400 r, each person's dose depending on his duties.

The *JF* group demands particular attention for two reasons: (1) It indicates that 13-day fallout radiation (the dose rate of which declines according to the decay law of fission products) induces the same clinical picture and the same time course of disease as short-term exposure. (2) It demonstrates that, during the latent phase, a crew is able to perform normal work and to accomplish all the tasks necessary for safe return of a boat in spite of the the fact that the ensuing bone marrow depression phase proceeds in a serious, or even grave, clinical course.

In summary, then, it can be stated that in the dose range from 200 to 400 r the clinical course of the acute radiation syndrome is predominantly serious or grave. All exposed persons will require hospitalization and intensive medical treatment. However, these measures, if they can be instigated properly, promise a favorable outcome and, most likely, recovery to a normal and vigorous life. Final judgment on this point must be held in abeyance until follow-up studies on the Japanese fishermen are available. The physician's efforts can be expected to be most rewarding in this dose range since, here, many lives can be saved.

Dose range: 401-600 r

As shown by the corresponding section in table 2, this range is documented by 3 cases only. Patients LA_4 and R_2 displayed typical pictures of the acute radiation syndrome, while patient LA_1 presented a fulminating clinical course which included gastrointestinal disturbances. A group of 4 hopelessly advanced cancer patients treated with whole-body x-irradiation by den Hoed et al.,[15] most likely, falls also in the upper part of this dose range; an exact classification is impossible owing to the technic and dosimetry employed. Of these patients, 3 died under circumstances indicative of the acute radiation syndrome. At that time, it had not yet been established that the maximal bone marrow depression will occur 4 to 6 weeks postexposure, and it was still considered safe to continue whole-body irradiation, with intervals of only a few days between each exposure, as long as the leukocyte count did not fall below 2,500 per μl. Thus the authors were completely surprised when about 3 weeks posttreatment granulocytes disappeared "almost completely," thrombocytes were "hardly present," hemorrhage from gum and nose appeared, and petechial bleeding in the skin became evident. Moreover, fever and infection complicated this picture of "agranulocytosis" and caused death of the patients between 3 and 7 weeks after cessation of radiotherapy. In addition, much of the *JBC* data can be assumed to fall in this dose range; there exist also numerous animal experiments that allow cautious extrapolation.

When all the direct and indirect evidence is taken into account, the following inference may be made: Up to about 500 r, the clinical course of the acute radiation syndrome is largely determined by radiation effects on the lymphoid tissue and the bone marrow—the most radiosensitive cell groups of the adult individual. Temporary depression of the gonads need not be considered in this regard since no serious constitutional reactions are involved. At doses above 500 r, however, direct radiation damage to the epithelium of the gastrointestinal mucosa—the next cell group in radiosensitivity—becomes a decisive factor. In the generative centers of the jejunal and iliac crypts, particularly, radiation causes arrest of mitotic activity. This production block of viable new cells, combined with decay of already existing cells, leads to denudation of the intestinal wall.[30] Functionally, the structural change has several serious consequences. As shown by Brecher and Cronkite,[31] water and electrolyte loss into the lumen of the alimentary tract may be so severe as to cause vascular collapse. Furthermore, denudation of the mucosa together with a defense mechanism weakened by bone marrow depression, leaves the organism wide open to invasion by toxic substances and bacteria. These factors, singly or combined, are responsible for the fulminating clinical course of the disease. In the fulminating forms a clear

latent phase is no longer present, and death may occur at any time during the first 3 weeks postexposure, while patients showing predominantly hematopoietic depression succumb, if at all, during the critical period extending from 3 to 6 weeks postirradiation.[32]

In summary, then, it can be stated that in the dose range from 400 to 600 r the clinical course of the acute radiation syndrome is predominantly grave. Up to 500 r, the bone marrow injury still determines clinical picture and outcome, whereas at higher doses direct damage to the epithelium of the gastrointestinal tract becomes more and more the decisive factor bringing about a fulminating course of the disease—the gastrointestinal form of the acute radiation syndrome.

The gastrointestinal form of the acute radiation syndrome is illustrated by one of the nuclear accidents, LA_3.[12, 33] The scientist involved was performing critical mass determinations. For that purpose two pieces of bomb material, hemispheres the size of a split baseball mounted on a rack, were slowly pushed toward each other. Neutrons from an outside source triggered in the fissionable material chain reactions that became more intense with narrowing air gap. Just before reaching the critical distance—and thus before an explosive build-up of chain reactions occurred—the hemispheres had to be separated. One day the bomb materials accidentally came too close together and the reaction in the critical assembly began to "run away," emitting massive amounts of penetrating ionizing rays. The scientist was exposed to a combined neutron, gamma, and roentgen radiation of about 2,000 r to the whole body. He experienced nausea within a few minutes, and he vomited before reaching the hospital about 60 minutes later. During the next few hours vomiting increased in frequency and one loose diarrheal stool was passed. From 12 hours postexposure onward these prodromal reactions ceased completely, and the general condition began to improve. The patient remained in satisfactory condition until the 6th day when a grave deterioration took place abruptly. The white blood cell count fell precipitously to very low values; the low-grade fever existing since the day of the accident rose suddenly above 102 °F; nausea, vomiting, and diarrhea reappeared; and signs of a severe paralytic ileus developed. The patient's major complaint was abdominal distention. No peristaltic sounds could be heard. By gastric suction 10 liters of a green fluid with fecal odor and appearance were aspirated within a 24-hour period. In spite of continuous gastric suction, parenteral fluid supply, blood transfusions, and antibiotic treatment, the deterioration progressed swiftly to beginning circulatory collapse on the 8th day and death on the 9th postexposure day. At autopsy, the most striking changes were found in the small intestine. "It was distended, flabby and filled with

dark-brown semiliquid material. The vessels were intensely congested, and there were numerous petechial hemorrhages on the serosal surface. The mucosal surface was edematous and deep red, particularly in the region of the jejunum where, in addition, the surface was covered with a membranous gray-green exudate that could be stripped off in sheets."[12] Histologic examination showed complete erosion of the jejunal and iliac epithelium with loss of the superficial submucosal layers. The denuded surfaces were covered by exudate containing masses of bacteria that, in the ulcerated portions, had invaded the intestinal wall. In essence, the anatomic diagnosis was then as follows: Diffuse membranous and ulcerative enterocolitis associated with aplasia and depletion of bone marrow, lymph nodes, and lymphatic system in spleen and gastrointestinal tract.

HIROSHIMA AND NAGASAKI

At 0815 hours on 6 August 1945, an atomic bomb was detonated approximately 2,000 feet above the city of Hiroshima, and 3 days later at 1102 hours another one was exploded over the city of Nagasaki under essentially the same conditions. Most of the population were either on the streets or in their rather lightly constructed homes and business establishments. In Hiroshima 70,000 to 80,000 persons died, and at least as many were injured. Since 72 of the 190 medical doctors residing in the city perished, and since most of the hospitals were destroyed, catastrophic conditions ensued with respect to care and treatment of the injured.[34] It is understandable that during the first week only the most critically injured patients could be retained and observed closely in the improvised clinical facilities. Most of these casualties, showing combinations of mechanical wounds, thermal burns, and radiation injury, succumbed rapidly.[2,3,34,35] Perhaps one seventh of the total number of injured persons escaped both mechanical lesions and burns, but received radiation doses sufficient to cause clinically significant sequelae.[35] These patients entered medical care in two waves. The first one, comprising predominantly persons exposed at a distance of less than 1,000 meters from the hypocenter, began to appear within a few days after the attack; its start merged with the influx of the numerous casualties showing combined injuries. In this first wave, severe gastrointestinal disturbances—tenacious anorexia, vomiting, and diarrhea associated with extreme weakness—were most conspicuous, predominating the entire clinical course. At the end of the first postattack week, serious leukopenia had developed in the patients still living and was complicated by high fever as well as profuse bleeding in almost every organ. Purpura, bloody diarrhea, bleeding from the gum, epistaxis, hematemesis, and hemoptysis, in this order of frequency were the most common forms of blood loss.[3,34,37] In one group of autopsies, subarachnoid hemorrhage was seen in

60 per cent of the cases.[35] The first wave of casualties had very poor prognosis; the clinical course was fulminating; practically all of these patients died within 2 weeks postexposure from dehydration with vascular collapse, or fatal bleeding, or septicemia.

The second wave of radiation casualties entered medical care about 3 to 4 weeks after the attack. Since by that time the worst confusion had subsided and the improvised clinical facilities had been much improved, and since the Japanese medical personnel had begun to understand the etiology of the unfamiliar disease,[34] clinical observations, laboratory examinations, and hospital records obtained on these patients, as compared to those on patients of the first wave, were much more complete and reliable. Generally, exposure had occurred in open air or in Japanese-type housing at a distance of 1,000 to 2,000 meters from the hypocenter; in the occasional instances where the distance had been less than 1,000 meters the individuals had been sheltered by heavy concrete buildings. This second wave of casualties displayed the "typical" acute radiation syndrome. A brief prodromal phase of 3 days' duration was followed by a latent period lasting about 3 weeks. During that time most of the patients continued to work; frequently they participated in the strenuous duties of clearing the rubbish of the city. In only a few instances was there a record of persisting weakness and easy fatigability. Approximately 2 weeks after the attack, the hair of the scalp became loose; this was considered an ominous sign.[34] A few days later general malaise, fever, purpura, and other typical complications compelled the patient to seek hospital admission. Hachiya,[34] director of the Hiroshima Communications Hospital, describes in his diary the following case as characteristic: The 28-year-old female patient had been inside a solid building at 700 meters from the hypocenter. Shortly after the bombing, she developed weakness, nausea, vomiting, general malaise, and diarrhea. Two days later these complaints had vanished and physical strength as well as appetite began to return. Thereafter, she ate plenty and did light work, although some fatigue and malaise persisted. On the 19th day, while combing, she noticed large amounts of loose hair. Recognizing this as a portentous sign, she asked for a physical examination on the 22d day. Nothing abnormal was found with the exception of severe weakness, epilation of about two-thirds of the scalp area, and marked leukopenia. She was admitted to the hospital where her condition deteriorated swiftly. In days postattack the sequence of events was as follows: 25th, petechiae and severe malaise; 29th, anorexia, increase in size and number of petechiae, and fever of 101.5°; 33d, weak pulse, and further enhancement of petechial bleeding; 37th, death.

Survey of the entire *JBC* data revealed a rather uniform clinical course for patients of the second wave.[2-4, 32, 35, 36, 38, 39] Around

the 20th day after the bombing, general malaise, pharyngeal pain, and ascending unremittent fever appeared. Within a few days, petechiae and ulcerative lesions of lips, mouth, and pharynx became manifest. Leukopenia and thrombocytopenia were most pronounced between the 3d and 5th week postexposure. During this period, representing clinically the critical phase of the illness, severe hemorrhage and overwhelming respiratory or enteric infection caused the death of about 50 per cent of the patients. In the survivors, recovery was heralded between the 5th and 6th week by cessation of the pharyngitis followed by disappearance of petechiae and fever, and finally by healing of the ulcerative lesions. This improvement was associated with an increase in circulating leukocytes and platelets, while red cell count and hemoglobin content of the blood generally continued to decline, reaching the minimum around the 6th and 8th week. Most patients became completely asymptomatic at 3 months following the attack.

Comparison of the *JBC* data with the experience gained from radiotherapy and nuclear accidents leads to several important conclusions. The first wave of casualties obviously represents the fulminating form of the acute radiation syndrome with direct radiation damage to the gastrointestinal epithelium as the determining pathogenic factor. It then follows that these patients must have been exposed to air doses in excess of 500 r. The second wave of casualties evidently represents the typical form of the acute radiation syndrome with hematopoietic depression as the determining pathogenic factor. These patients, therefore, must be assumed to have been exposed to air doses ranging from 200 to 500 r. These conclusions, compelling as far as the clinical symptomatology is concerned, do not agree with dose estimates calculated from physical considerations. These calculations do yield doses higher than 500 r for the area described around the hypocenter by a radius of 1,000 meters, but they arrive at only 15 r for a distance of 2,000 meters where the clinical picture demands at least 200 r. This obvious discrepancy between medical and physical dose estimates has already attracted attention and speculation about its cause.[40] In the present report, precluding the treatment of technical dosimetric problems, this interesting phenomenon cannot be analyzed. The physical factors involved have been re-examined in a recent study of the bomb data.[41]

SUMMARY OF DOSE-EFFECT RELATIONSHIP, AND DEFINITION OF CLINICAL THRESHOLD OR HOSPITALIZATION DOSE IN MAN

When for a large group of whole-body irradiated animals the mean survival time is plotted as a function of dose, the graph does not proceed in a smooth curve but forms three distinct steps.[42] Furthermore, it can be shown that these steps reflect three different pathogenic mechanisms. Death is caused, in the

low dose range, by hematopoietic depression; in the middle dose range, by gastrointestinal denudation and inflammation; and in the high dose range, by failure of the central nervous system. Although the corresponding data are largely unknown for man, they can be extrapolated with reasonable accuracy from clinical findings and animal observations. Because of the close agreement of radiation-induced effects among the various species of the mammalian class, man can be expected to show the three-step survivaltime curve depicted in figure 2. Correspondingly, three different types of clinical pictures should exist, and the

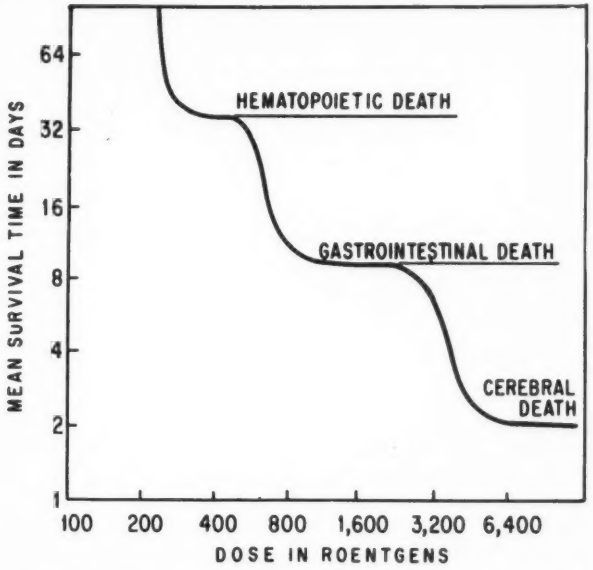

Figure 2. Mean survival time of a large group of persons exposed to various amounts of ionizing radiation. The curve is extrapolated for man from clinical data and animal experiments.

acute radiation syndrome should be subdivided, as shown in table 3, into hematopoietic, gastrointestinal, and cerebral forms. In man, the hematopoietic form of the disease is rather well established—based on a sufficient number of careful observations; the gastrointestinal form is but vaguely understood since only two nuclear accidents fall in this range and since *JBC* records of early cases are not complete; and the cerebral form is completely unknown because (1) persons of the *JBC* group who were close enough to the hypocenter to receive such high doses, necessarily experienced also lethal thermal burns or mechanical injuries and (2) patients of this group were lost

during the confusion of the first 3 days postattack without examination and recording.

TABLE 3. *The acute radiation syndrome*

	Cerebral form	Gastrointestinal form	Hematopoietic form
Threshold dose	2,000 r	500 r	100 r
Characteristic signs and symptoms	Convulsions; tremor; ataxia; lethargy	Diarrhea; fever; disturbance of electrolyte balance	Leukopenia; purpura; hemorrhage; infection
Time of death	Within 2 days	Within 2 weeks	Within 2 months

For the sake of completeness (the hematopoietic and the gastrointestinal forms having been treated earlier), an attempt must now be made to predict and describe for man the cerebral form of the disease as it emerges from animal experiments. Weakness, drowsiness, and listlessness—components of the prodromal complex already at low-level irradiation—will develop within 1 hour after exposure and will proceed swiftly to severe apathy, prostration, and lethargy. Over this progressive loss of physical and mental activity is superimposed, particularly during the first 3 hours postexposure and at doses in excess of 5,000 r, a disturbance of the motor system. In short intervals seizures will occur either in form of generalized muscle tremor, or ataxic movements, or full-blown epileptoid convulsions of the grand mal type.[43] Patients who survive the convulsive phase will be prostrate and somnolent, and will expire within 2 or 3 days postexposure. The anatomic substrate for the progressive loss of physical and mental activity must probably be sought in widespread inflammatory foci that begin to develop within 1 hour after irradiation. These nonbacterial radiation-induced reactions form the pictures of meningitis, encephalitis, and vasculitis, and are soon associated with brain edema. The convulsive seizures, on the other hand, are most likely related to pyknosis occurring in the granule cell layer of the cerebellum within 2 hours postexposure.[32, 43]

Obviously the three characteristic forms of the acute radiation syndrome will be separated from each other by broad dose ranges of transition where mixed effects will result. These more complex clinical pictures, however, become explainable when the pure forms are understood clearly. From a practical medical standpoint, it should be reiterated that, so far, the pure hemato-

poietic form and clinical pictures representing a transition from the hematopoietic toward the gastrointestinal form have predominantly been encountered in bomb explosions and nuclear accidents. For future disasters it may be assumed that these forms again will represent the major medical problem; the ensuing sections will, therefore, be restricted to further analysis of these pictures only.

Ionizing radiation, as many other physical and chemical factors brought about or intensified by modern civilization, is supposed to be biologically harmful regardless of dose. Obviously, it is only a matter of time until there exist laboratory methods refined enough to detect the minute functional changes possibly induced by very low doses. Such alterations, unless usable as biologic dosimeters, have no bearing on the casualty problem. Also negligible are the minor systemic reactions occurring in the low dose range. What really matters is the threshold dose beyond which the clinical course is such that hospitalization becomes necessary for an appreciable number of persons among a large irradiated group. When a military installation or a city has been exposed to a known air dose, the medical countermeasures for a dose beneath the "hospitalization threshold" will be different from the one above it. In the first case, psychologic reassurance and taking white blood cell counts, as a precautionary measure, may be the only things required. In the second case, elaborate steps can be taken to prepare beds and medical supplies for the anticipated number of casualties since, owing to its relatively long latent phase, the actual disease will start several weeks postexposure. Therefore, good organization and logistics may be of primary importance. From the previous analysis of data—showing that the hospitalization threshold lies near an air dose of 200 r—figure 3 was designed for "typical" cases exposed to various amounts of radiation.

RELATIVE IRRELEVANCE OF TYPE OF PENETRATING IONIZING RADIATION FOR THE CAUSATION OF THE ACUTE RADIATION SYNDROME

To the medical officer the physical aspects of the radiation problem appear, at first glance, to be of embarrassing complexity. Biologic injury may be inflicted by high-speed particles, the various types of which are steadily increasing with progressing knowledge of the nuclear structure, and it may also be induced by high-energy photons covering the electromagnetic wave spectrum from ultraviolet to the hardest gamma radiation. Moreover, a specified amount of radiant energy may be transferred to the organism within seconds as in exposure to the atomic bomb, or it may be transmitted over a period of time measured in days, weeks, or even years as in exposure to fallout from the hydrogen

bomb. Finally, the radiation source may be located at various distances from the subject, or it may be attached to the skin as in fallout contamination, or it may have its seat in internal organs as a consequence of ingestion or inhalation of radio-

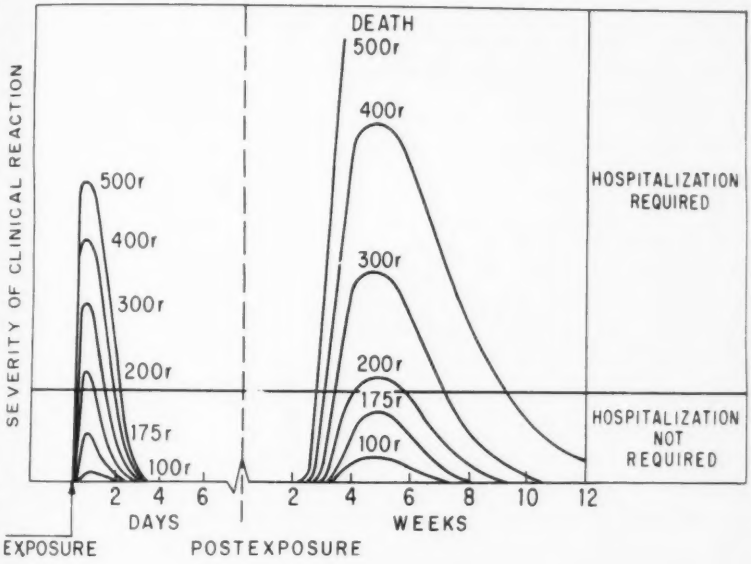

Figure 3. Clinical course of the acute radiation syndrome in "typical" cases exposed to various amounts of penetrating ionizing radiation. The horizontal line indicates the "hospitalization threshold."

active substances. From a practical medical standpoint, fortunately, this complexity can be reduced to but a few realistic situations. Although one case of suicide with large amounts of thorium-X proves that the typical acute radiation syndrome can be elicited by the uptake of radioactive substances,[44] present-day experience indicates that internal irradiation from fallout material is much too small to trigger the acute radiation syndrome or to influence its course.[32] External irradiation, when composed of soft roentgen, alpha, or beta rays, will be absorbed predominantly in the skin and will produce in this organ inflammatory reactions frequently progressing to ulcerative lesions. This disease—the acute radiation dermatitis—has been excellently described as a consequence of fallout contact,[7] but it cannot be covered in the present report. External irradiation, when composed of hard roentgen, gamma, neutron, or other penetrating rays, will cause the acute radiation syndrome. The severity of the clinical reaction is essentially the same, regardless of whether a certain dose is delivered within a microsecond or

over a period of 4 days; an estimate shows that in the latter case the "biologic efficiency" is decreased by less than 6 per cent.[45] When the time of exposure is extended beyond 4 days, however, the air dose necessary to cause the acute radiation syndrome increases appreciably with length of exposure time. Therefore, to avoid drastic systemic reactions, radiotherapy applies fractionated doses, each partial dose being separated from the next one by an interval of several weeks. Observations on patients treated with the Heublein technic[16] also demonstrate that the clinical tolerance threshold drifts to higher dose levels for protracted exposure as compared to one of less than 4 days' duration. Craver[20] reached the conclusion that advanced cancer patients withstand up to 300 r total-body exposure when given over a period from 20 to 30 days and that the lack of systemic effects, other than those caused by the progressing disease, indicates that such doses may be well tolerated by healthy persons. A dose of 300 r, given in one continuous course for 10 days, produces definite responses and is about the highest whole-body exposure that can safely be administered.[17, 46] When the constitutional reactions in the latter patients are compared with those of the *MDA* series, it appears that 300 r given during a period of 10 days correspond approximately to 200 r applied in 51 minutes. Evidently this shift in threshold necessitates, for long-term exposures, that the accumulated air dose be multiplied by a factor smaller than unity to obtain the "effective dose" from which prognosis of the expected biologic consequences can be made; however, exact size and time function of the factor are still unknown for man.[45] Large-scale comparative studies with the Heublein technic and the *MDA* procedure should enable determination of these elements so important in the case where a population is forced to occupy permanently an area contaminated with fallout, under which condition there is a marked difference between air dose and effective dose. When people, as the *JF* group, have to stay no longer than 2 weeks in the contaminated environment, the discrepancy between the 2 doses is less striking, and the correction factor deviates but slightly from unity. Calculation, based on the decay law for fission products, shows that during the first 4 days more than 75 per cent of the total dose emitted throughout the 2-week period has been received. If evacuation can be effected within 4 days after the beginning of fallout, as in the *MI* groups, the uncorrected air dose can be considered as the effective dose. *In summary, then, it can be stated that all types of penetrating ionizing radiation, singly or combined, produce one specific clinical picture—the acute radiation syndrome; for exposure times extending beyond 4 days, the biologically effective dose will be smaller than the measured air dose.*

To emphasize the validity of the previous statement, two sets of data will be discussed—namely, hematology and case histories of a few representative practical examples. In figure 4, the time course of the white blood count is depicted for four different situations involving penetrating ionizing radiation.

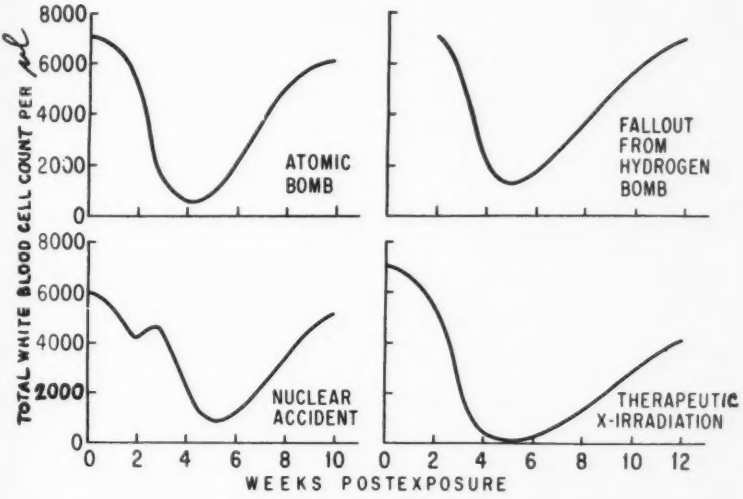

Figure 4. Similarity of the leukocyte response in persons exposed to various types of penetrating ionizing radiation. Origin of data is explained in text.

The origin of the individual curves is as follows: atomic bomb, a group of Hiroshima casualties;[47, 48] fallout from hydrogen bomb, one Japanese fisherman—case Bikini-H in reference 10; nuclear accident, case R_2; and therapeutic x-irradiation, *MDA*, patient 34. Comparison of the curves reveals a striking similarity; in all instances the minima lie between 4 and 6 weeks postexposure. The transitory recovery, occurring in the nuclear accident between weeks 2 and 3, is not characteristic for this special case because it is seen quite frequently after exposure to various types of penetrating ionizing radiation. For the sake of clarity, lymphocyte, thrombocyte, and erythrocyte counts have been omitted from figure 4. When compared with the white blood cell count, the lymphocyte count declines consistently earlier and more abruptly, and its recovery is delayed; the thrombocyte count presents a time course closely parallel to that of the white blood cell count; while the erythrocyte count decreases much more slowly and reaches its lowest value several weeks later. In the four circumstances depicted in figure 4, the causative agents are a mixture of gamma photons and neutrons for the atomic

explosion and the nuclear accident; gamma photons of various penetrating powers, combined with alpha and beta components causing radiation dermatitis, for the fallout case; and x-rays for the therapeutic exposure. Yet, in spite of this diversity, the biologic changes are surprisingly uniform. Thus, figure 4 underlines once more the fact that the hematologic response is the same regardless of the type of radiation by which it is elicited. Apparently, ionizing radiation triggers in the hematopoietic tissues a process that then proceeds according to inherent properties of that biologic system. This uniformity of response is even more accentuated by the following excerpts from a few typical case histories.

Atomic bomb radiation (JBC). At the time of the Hiroshima explosion, a 25-year-old soldier was on the upper floor of a two-story Japanese building located about 1,000 meters from the hypocenter, but he was able to leave the city for shelter in the fields. On the day after the the attack, although experiencing malaise, he returned to his garrison. On the 4th day he resumed his normal duties involving strenuous exercises on the drill field and a 10-mile march. Even though epilation, noticeable from the 14th day onward, indicated serious exposure, he continued work until the 21st day when chills, a feverish feeling, and weakness appeared. Petechiae developed 24 hours later, and hospitalization became necessary on the 24th day. On admission he complained of headache, malaise, and pain in the oral cavity. Beginning with the 26th postattack day, pharyngitis with high fever dominated the clinical picture; moreover, there was swelling of the gingiva, superficial ulcerations around the angles of the mouth, and dysphagia. After the fever had subsided on the 39th day, petechiae as well as inflammatory reactions began to clear, and he was discharged on the 60th day after the explosion when his white blood cell count had risen to 1,400 from a low of 900 per μl. Following release from the hospital he resumed work on his own farm.

Nuclear accident (R_2). A 21-year-old male patient accidentally received 450 r whole-body gamma and neutron irradiation from an experimental reactor when rules of operation were violated. Within a few minutes after exposure, pronounced weakness, headache, and vertigo developed and were swiftly followed by anorexia, nausea, and vomiting. This burst of initial reactions, reaching a maximum during the first 24 hours, lasted 3 days. Thereafter the general condition of the patient improved markedly and remained satisfactory until the 19th day when, rather abruptly, deterioration began. Recurrent chills accompanied by shivering, high fever, sore throat, petechiae, and frank hemorrhage from the gums appeared and were soon followed by an extensive ulcerative lesion comprising the right tonsil. This very grave clinical picture persisted throughout a period of 2 weeks, then recovery became noticeable. Fever disappeared on the 35th postexposure day and petechiae, inflammatory reactions, and frank bleeding had ceased by the 41st day.

The total white blood cell count, having been at a minimum of 150 per μl on the 28th day, returned to almost normal values. At the end of the 3d postexposure month the patient was released from the hospital and, following a 4-week vacation, he was able to resume his normal duties.

Therapeutic x-irradiation (MDA, patient 34). This 55-year-old male patient had Hodgkin's disease with lesions in lungs, ilium, 12th rib, and 12th thoracic vertebra. Since several courses of limited field roentgen therapy yielded only temporary amelioration, whole-body exposure to a nominal air dose of 200 r was administered in one session. Shortly after completion of the treatment, the patient experienced severe nausea, vomiting, and extreme weakness, necessitating antiemetic therapy with 25-mg doses of chlorpromazine hydrochloride, at 6-hour intervals. Even under this medication he vomited 7 times on the day of irradiation, and 4 times the following day; thereafter he became asymptomatic with the exception of light nausea on the 3d postradiation day. This favorable condition persisted for 3 weeks. On the 24th postradiation day, low grade fever and profound pancytopenia began to develop. Soon multiple gluteal abscesses as well as ulcerating lesions involving gingiva and hard palate appeared and progressed in spite of treatment with penicillin, streptomycin, and tetracycline hydrochloride (Achromycin®). Finally after beta-hemolytic *Micrococcus pyogenes* (var. *aureus*) resistant to tetracycline hydrochloride had been found on culture, improvement took place under administration of erythromycin. The patient became afebrile on the 51st day postradiation; soon thereafter the infectious lesions began to heal, and the leukocyte count rose to 2,300 from a previous minimum of 100 per μl.

Fallout from thermonuclear device (history of a clinically subthreshold case). This 26-year-old mother of four children, a native of the Rongelap Atoll, was exposed to about 175 r of penetrating fallout radiation as an aftermath of the thermonuclear test explosion at Bikini on 1 March 1954.

Approximately 4 to 5 hours after the explosion, a white material of snowlike appearance fell upon the island located 120 miles from Bikini. The natives, not aware of the significance of these "snowflakes" that continued to fall for about 1 hour, carried on their everyday life in the lightly constructed palm houses and out of doors. At 50 hours after the explosion, evacuation was executed by air and surface transportation to the Kwajalein Naval Station. Here, clothes were removed and laundered, while skin and hair were washed repeatedly with fresh water and soap.

On the day following the fallout, this particular patient was nauseated but did not vomit; she also experienced itching and burning of the skin presumably caused by direct contact with fallout material. These complaints soon disappeared and at the time of evacuation, 2 days after the beginning of exposure, she was feeling well. This favorable general condition, interrupted by a brief episode of upper respiratory infection, persisted throughout the entire observation time of 3 months

during which period she gained 2 pounds in weight. At several follow-up examinations, covering 3 years to the present time, no diseases other than occasional colds were reported, and no complaints interpretable as radiation effects were disclosed. She has had two additional pregnancies that were uncomplicated and led to the birth of two healthy babies at full-term. Since the first of these children was born in January 1955, conception must have occurred in April 1954, that means between 1 and 2 months postexposure. The hematologic findings on this patient (compiled in table 4) show a pronounced minimum of platelets around days 26 and 30, while a corresponding sharp dip of the white blood cell count probably was obscured by the intercurrent infection of the upper respiratory tract.

TABLE 4

Effect of exposure to penetrating fallout radiation on white blood cell and platelet counts of a 26-year-old female native of Rongelap Atoll

Days after beginning of exposure	Total WBC 1,000/μl	Neutrophils in percent of total WBC	Lymphocytes in percent of total WBC	Platelets in 1,000/μl
9	6.2	57	35	150
12	5.2	65	24	—
15	5.9	71	23	160
18	5.8	65	33	105
22	6.8	57	40	120
26	3.3	59	29	60
30*	10.0	64	32	50
33	5.7	54	38	130
39	5.9	76	22	160
43	4.1	50	48	240
47	4.5	62	36	180
51	3.8	46	50	135
54	3.0	49	51	120
62	6.9	—	—	160
2 years	9.0	63	34	188

*Upper respiratory infection.

This case history is of particular interest because it demonstrates that a dose close to the clinical threshold may cause nausea followed by definite hematologic alterations; whereas, general condition, feeling of well-being, physical activity, and capability to bear children are not affected.

ROLE OF PENETRATING IONIZING RADIATION AS A CASUALTY-CAUSING AGENT

Although the atomic explosions over Japan may have had revolutionary impact on military and political planning, their influence on medical concepts was far less striking. In many respects, the problems posed by the great number of casualties were not essentially different from those observed after large-scale bombing raids with conventional explosives. Ionizing radiation was a minor complication; heat and blast were really devastating. From a military medical standpoint, therefore, atomic bombs could be conceived as huge conventional bombs with some unusual side effects. It was the explosion of the first hydrogen bomb at Bikini in 1954 that revolutionized medical thinking. The aftermath of this event can still be felt, and its full meaning must be recognized by everybody concerned with medical problems under catastrophic conditions. Emphasized by the accidental exposure of the Marshall Island population and the Japanese fishermen, the Bikini explosion demonstrated that ionizing radiation can become *the* casualty-causing agent. Fallout from the bomb may cover thousands of square miles and deposit radioactive material of sufficient activity to be supra-threshold for the acute radiation syndrome. This means that a military installation or a city situated hundreds of miles away from a hydrogen bomb explosion will experience neither thermal nor blast effects, and may not even have knowledge of the disaster.

Yet, owing to the prevailing meteorologic conditions, several hours after the explosion, fallout may descend upon the area and expose its population to high amounts of penetrating ionizing radiation. Quite in contrast to Hiroshima and Nagasaki, the medical practitioner would then face a type of mass casualty completely different from that seen after conventional bomb attacks, and the countermeasures would have to deviate correspondingly.

Although the fallout problem has been thrust into medical and public attention by the first hydrogen bomb explosion, it should be pointed out that the phenomenon is not necessarily characteristic of this type of weapon (in the present report the popular term "hydrogen bomb" has been used as a synonym for the more general designation "thermonuclear bomb"). The difference between atomic and hydrogen bomb, in this respect, is one of degree rather than of kind. Furthermore, the amount of fallout depends strongly on the physical conditions under which a nuclear explosion occurs. Two extreme possibilities will be considered. First, the bomb explodes at a relatively high altitude above ground. In the process of detonation, a large amount of

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neutron and gamma radiation is released and transmitted to the earth below. At ground level the intensity of this "initial nuclear radiation," emitted within the first minute, will be determined essentially by the inverse square law and the absorption in air. At the point of explosion, a temperature of several million degrees exists and vaporizes the highly radioactive fission products as well as the unsplit fissionable material, casing, and other parts of the weapon. These hot gases form a highly luminous sphere—the "fireball"—that quickly expands to a diameter of about 200 feet for the atomic bomb and to 8,000 feet for the hydrogen bomb. As the fireball (rising with a rate of roughly 250 to 350 feet per second) cools, the vapors condense and the highly radioactive bomb debris is dispersed in the upper layers of the troposphere. The fine radioactive particles are then carried over appreciable distances and slowly descend to earth. Because of its considerable dispersion and late descent, this "worldwide fallout" conveys only minute amounts of radioactive material to the unit of surface area and the thereby emitted "residual nuclear radiation" is much too small to cause acute biologic effects. The conditions just described existed at Hiroshima and Nagasaki; therefore, radiation injuries were caused by the "initial nuclear radiation," while "residual nuclear radiation" was negligible.

Quite a different situation prevails when the explosion occurs at such a low altitude that the expanding fireball touches ground. By its million-degree temperature, rock, soil, and other material are vaporized and added to the above-described components. It has been estimated that 20,000 tons of surface substance may thus be vaporized and incorporated in the fireball of a thermonuclear bomb; the amount is less in case of an atomic bomb. Under the intense neutron irradiation during detonation, all of this material becomes radioactive. In addition, the rising fireball causes high winds at the earth's surface and thereby sucks up additional dirt and dust. As the terrific updraft started by the rising fireball subsides, the radioactive particles and contaminated soil material begin to fall gradually back to earth; the heaviest fragments touch ground close to the explosion site, the fine dust falls out later and farther away.[49] This highly radioactive "local fallout," covering in the Bikini explosion 7,000 square miles, causes such a large amount of "residual nuclear radiation" that, as demonstrated by the several accidents, it may well be suprathreshold for the acute radiation syndrome and, therefore, may become one of the most devastating casualty-causing agents.

VARIATION OF THE ACUTE RADIATION SYNDROME WITH INDIVIDUAL SUSCEPTIBILITY

Individual sensitivity to ionizing radiation varies markedly. Although exact figures are not available, a reasonably correct

estimate can be obtained and extrapolated from the *MDA* series, the *MI* population, and several groups of Hiroshima workmen[3] since in these instances large numbers of persons were exposed under almost identical conditions. These data lead to the impression that the extremes in susceptibility differ approximately by a factor of 2; for example, among a large group exposed to 200 r, the most radiosensitive person will develop a clinical picture of the same severity as that exhibited by the most radioresistant person among a group exposed to 400 r. Or, 300 r may be expected to be lethal to the most radiosensitive individuals, while about 600 r may be assumed to be the border line beyond which even the most radioresistant individual cannot be expected to survive. The reason for this wide difference in radiosensitivity, existing also among laboratory animals, is unknown; age, sex, state of nutrition, and many other factors have been studied in animal experiments without supplying an explanation. When for a large series of identically exposed persons the distribution curve is drawn with respect to clinical course—or more objectively to degree of white blood cell depression—a bell-shaped pattern is obtained, as suggested by the above-mentioned groups. With increasing dose, this curve will move toward a more severe clinical course (fig. 5) or lower white blood cell value. In figure 5, the LD_{100} for man has been supposed to be 600 r, consistent with most literature reports.[49] Although this value appears to be a reasonable assumption, it should be emphasized that there

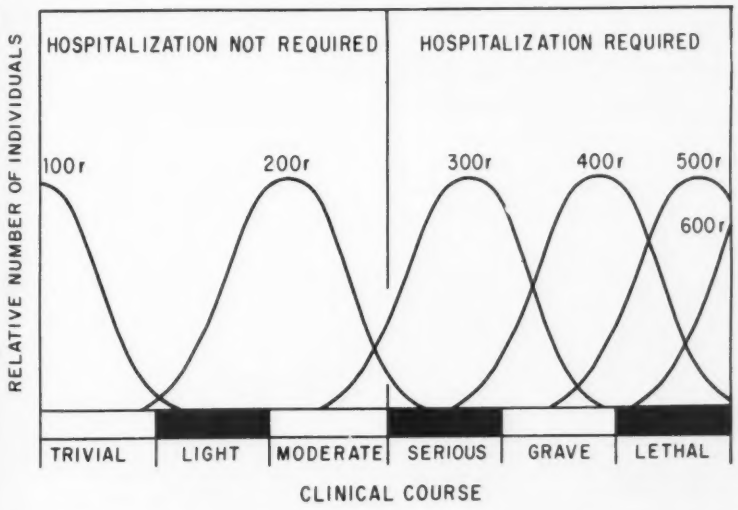

Figure 5. Effect of various amounts of penetrating ionizing radiation on the distribution curve with respect to clinical course. Data for human populations have been derived and extrapolated from clinical observations and animal experiments.

exist no human data establishing the border line for survival definitely at 600 r. When in figure 5 the area is determined between abscissa axis and that section of each dose curve which corresponds to a certain degree of clinical course, and when the ratio is calculated for this area to that of the corresponding entire distribution curve, a separation of casualties in per cent of their total number is obtained for each dose, as shown in figure 6. The heavy horizontal line through the middle of figure 6 represents the *hospitalization threshold.* It must be underlined

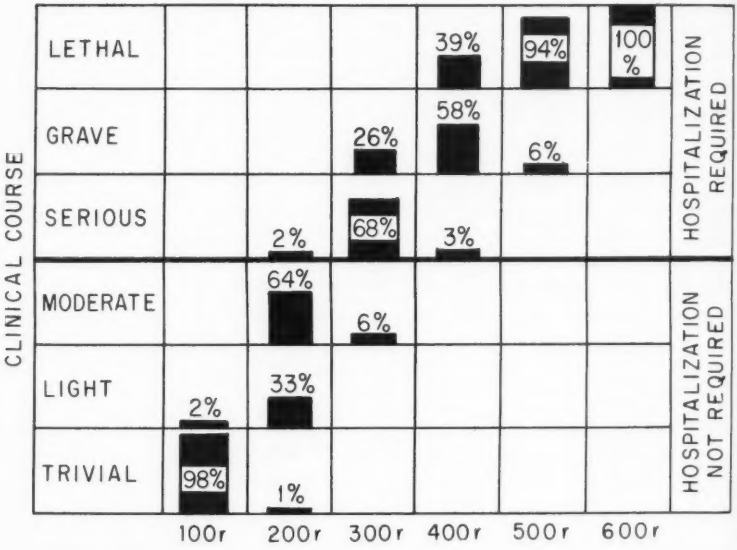

Figure 6. Estimate of casualty distribution for various doses of penetrating ionizing radiation and for various degrees of severity of clinical course. The data are derived from figure 5.

that this threshold, according to all human data available, is rather sharply defined. Moderate bone marrow depression is surprisingly well tolerated and apparently is associated with no complication other than an increased fatigability. In sharp contrast, serious bone marrow depression leads, after the latent phase, to the sudden onset of the fully developed hematopoietic form of the acute radiation syndrome, requiring immediate medical attention. Figure 6 yields the following information: Suppose a large population has been exposed to an air dose of 300 r. Logically, this dose would refer to the air surrounding each person who may be located in the open, in a house, or in a shelter; that means it would refer to the dose shown by the dosimeter worn by each individual. Six per cent of this population

would require precautionary surveillance only; whereas 94 per cent would have to be hospitalized at the end of the latent phase. Sixty-eight per cent of the population are expected to enter a serious clinical course followed predominantly by complete recovery; while 26 per cent are expected to exhibit a grave clinical course ending frequently in death.

From the standpoint of medical logistics, it is important to estimate incidence, onset, and duration of hospitalization as anticipated for an exposed population. When the data on dose dependency of the clinical course (discussed earlier) are combined with those on individual susceptibility, a graphic representation of such an estimate can be obtained (fig. 7). To demonstrate the significance of figure 7, it shall be assumed that a large population has been exposed to 250 r. For this dose,

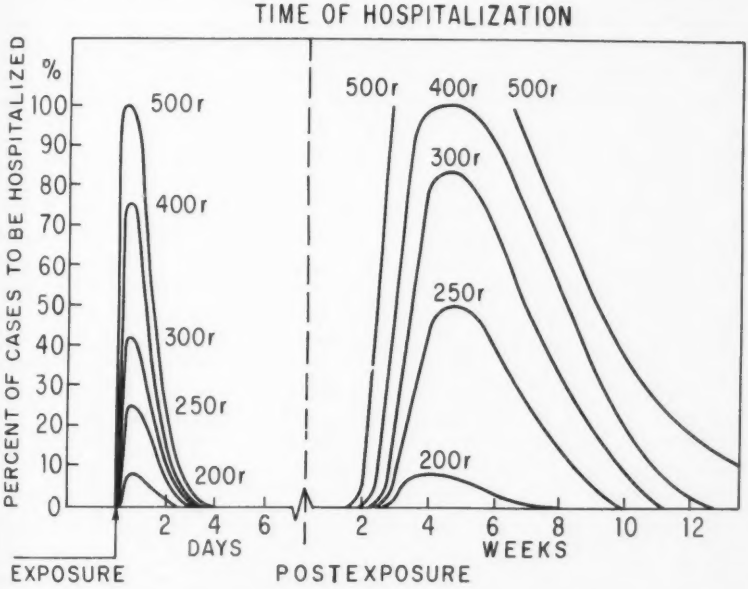

Figure 7. Estimate of incidence and duration of hospitalization for populations exposed to various amounts of penetrating ionizing radiation.

figure 7 indicates that approximately 25 per cent of the people would be hospitalized during the first 2 days after exposure. Of course, this might not be feasible under catastrophic conditions where the short period of hospitalization might not justify the efforts required to transfer a large number of casualties; however, these persons would certainly require close medical attention. The large influx of patients to hospitals could be

expected to occur 2½ weeks postexposure. At the height of the disease—4 to 5 weeks postirradiation—about 50 per cent of the population would require hospital treatment. Thereafter, the number of in-house patients would be expected to decline rather rapidly, with the last patient leaving the hospital at 10 weeks postexposure. In a similar fashion, figure 7 may be used to estimate incidence, onset, and duration of hospitalization for other dose levels. It must be stressed that the curves of figure 7 are based largely on extrapolation. Therefore, future additional information will make correction possible, but adjustments are expected to affect only minor details without changing the basic design of the figure.

INTERRELATIONS BETWEEN SIGNS, SYMPTOMS, AND DOSE LEVEL

When a group of persons has been exposed to an unknown dose of penetrating ionizing radiation, diagnosis and prognosis must be based on developing signs and symptoms; the most important ones will be briefly discussed and evaluated.

Nausea and Vomiting

Absence of these prodromal effects is of eminent prognostic significance. It indicates, with high probability, that the air dose was less than 100 r, that the ensuing clinical course will be trivial in most cases, and that need for hospitalization will not arise. On the other hand, presence of these prodromal effects, even very early after exposure, does not imply poor prognosis, as frequently stated. It strongly indicates, however, an air dose in excess of 100 r and, therefore, development of the acute radiation syndrome in most instances. Severity and outcome of the disease cannot be predicted from time of onset and degree of initial reactions since the two complexes are only loosely related. Nevertheless, persons showing prodromal symptoms should be closely watched for the appearance of further manifestations of the radiation insult.

Latent Phase

Onset of the disease after a 3-week latent period, following remission of the initial reaction, heralds the typical uncomplicated hematopoietic form of the acute radiation syndrome. In the majority of cases complete recovery may be achieved by proper management of the patients. Conversely, when a clear latent phase is not evident, or when its duration is much shorter than 3 weeks, the early development of the illness foretells a grave clinical course probably complicated by gastrointestinal involvement. Prognosis is then poor.

Fever

Stepwise ascending fever starting around the 20th day post-exposure, even when associated with petechial and frank hemorrhage as well as with oropharyngeal infection, is typical for the pure hematopoietic form of the acute radiation syndrome and does not necessarily compromise its favorable outcome. In sharp contrast, high fever developing within 2 weeks post-exposure is a poor sign. With great probability it indicates gastro-intestinal involvement since, most likely, it is a consequence of bacterial toxins or of bacterial invasion originating from the alimentary tract. The clinical course then must be expected to be grave and the outcome very dubious.

Epilation

Loss of hair, when definitely caused by penetrating ionizing radiation, and not by alpha or beta emitters contained in fallout contamination of the skin, indicates an air dose in excess of 300 r. It is common radiotherapeutic experience that about 300 r are the smallest dose to cause temporary epilation. This sign is of prognostic importance for two reasons: (1) Generally it becomes noticeable as early as the end of the 2d postexposure week; that means it appears about 1 week before start of the actual disease, thus allowing sufficient time for precautionary measures. (2) After an exposure to more than 300 r a serious or grave clinical course must be expected; hence, epilation is the forerunner to the need for hospitalization. Therefore, all persons observing excessive loss of hair after exposure to penetrating ionizing radiation should be kept under close medical surveillance.

Diarrhea

Although transitory loose stool or diarrhea may occur occasionally as part of the prodromal reaction, they are not characteristic traits of the uncomplicated acute radiation syndrome. Opposing statements probably are derived from the fact that diarrhea was rather frequently observed among Hiroshima and Nagasaki casualties. Close scrutiny reveals, however, the widespread existence of this disturbance in the population of the two cities even before the attack. Nuclear accident and radiotherapeutic data prove beyond any doubt (see tables 1 and 2) that diarrhea does not belong to the symptomatology of the hematopoietic form of the acute radiation syndrome. Contrariwise, early and persistent diarrhea, when definitely not caused by malnutrition or accidental infection, is a rather serious sign. Very likely, it indicates exposure to more than 400 r and the existence of severe gastro-intestinal damage. Prognosis is, at best, dubious.

Leukopenia

As long as the total white blood cell count stays above 2,500 per μl, overt disease is not anticipated. Such a degree of radiation-induced leukopenia is, in general, well tolerated and, with the exception of increased fatigability, does not seriously affect physical activity. When the count ranges between 2,500 and 1,000 per μl, the typical acute radiation syndrome will appear in most instances. Close attention is required with regard to the development of purpura, hemorrhage, and infection. Under proper treatment, prognosis is favorable. Counts below 1,000 per μl always will be associated with a serious or grave clinical course. The fact that in Hiroshima and Nagasaki leukopenias of such degree generally heralded fatal outcome, is applicable only to practically untreated cases under catastrophic conditions. With suitable treatment in modern hospital facilities, even white blood cell values as low as 100 per μl may be handled successfully, as demonstrated by radiotherapy patients and nuclear accident victims. It should be reiterated that in the pure hematopoietic form of the acute radiation syndrome the minimal white blood cell count is encountered between weeks 4 and 6, and the cell drop frequently occurs rather abruptly. Therefore, in all persons suspected of having been exposed to appreciable amounts of penetrating ionizing radiation, hematologic examination must be performed regularly for 3 months, with particular emphasis on the critical time period extending from the 20th to the 40th day postexposure.

Lymphopenia

The following dose ranges are probably indicated by the lymphocyte count during the first 48 hours postexposure; less than 50 r, when there is no significant decrease; less than 100 r, when the decrease is mild; and a dose in excess of 100 r, when the lymphocytes fall below 50 per cent of normal values.

TREATMENT OF THE ACUTE RADIATION SYNDROME

Since the therapeutic management of the acute radiation syndrome has been ably described by Cronkite,[50, 51] the ensuing brief survey essentially summarizes his views, with minor additions and modifications.

Prodromal Complex

Most important is psychologic reassurance emphasizing the transient nature of the disturbance as well as its relative insignificance with respect to the actual injury. In more serious cases, additional administration of sedatives is indicated—for example, chlorpromazine hydrochloride in oral doses of 25 mg every 6 hours. Only occasionally will vomiting be so profuse as to necessitate parenteral replacement of fluid.

Cerebral Form

No experience is available excepting the fact that in animal experiments heavy sedation eliminates convulsive seizures.

Gastrointestinal Form

Since the alimentary tract will not tolerate anything other than small quantities of fluid, parenteral nutrition is mandatory. Water and electrolyte equilibrium must be maintained by large amounts of intravenous saline-glucose, plasma, and balanced electrolytes. Around the end of the 1st postexposure week, when high fever and infection are expected to occur, antibiotic treatment should be started. Excellent nursing care and aseptic technic are paramount. Frank hemorrhage, anticipated during the 2d week, will require transfusions of fresh whole blood.

Hematopoietic Form

Infection being the principal complication, careful examination of body temperature and oral cavity are necessary, particularly from the 3d postexposure week onward. The slightest evidence of infection is an indication for beginning antibiotic treatment. Cronkite does not recommend prophylactic administration of antibiotics because of two hazards—sensitization of the patient, and development of bacterial resistance. Purpura and frank hemorrhage require repeated transfusions of fresh whole blood or separated platelets and leukocytes. Frequency and amount of transfusions will be determined by the blood count. It may be worthwhile to try additional procedures in accordance with the usual management of agranulocytotic disorders. Figure 8 presents a graphic survey of the acute radiation syndrome in its hematopoietic form. The temporal relationship has been depicted for clinical course and therapeutic methods as applied in the *JF* group and the *MDA* series.

Some remarks concerning the effectiveness of the outlined therapy, especially that of the hematopoietic form, should be added. The frequently advanced concept of the treatment as purely symptomatic is too pessimistic. Hematopoietic depression and denudation of the gastrointestinal mucosa generally are transient, as are radiation-induced epilation and azoospermia. Therefore, the therapeutic goal must be to help the patient overcome the relatively short period of time during which his own organism is not able to supply the critical cell elements. Hence, the transfusion procedures represent an actual substitution therapy. This fact can be demonstrated strikingly in animal experiments. In rats the minimal white blood cell count occurs around the 8th day postexposure. Parabiosis between an irradiated and a nonirradiated rat will carry the exposed animal through the bone marrow depression phase when adequate cross-circulation exists

between the 4th and 10th postexposure days; longer parabiosis does not add to the beneficial effect.[52] It is very likely that markedly improved treatment of the acute radiation syndrome

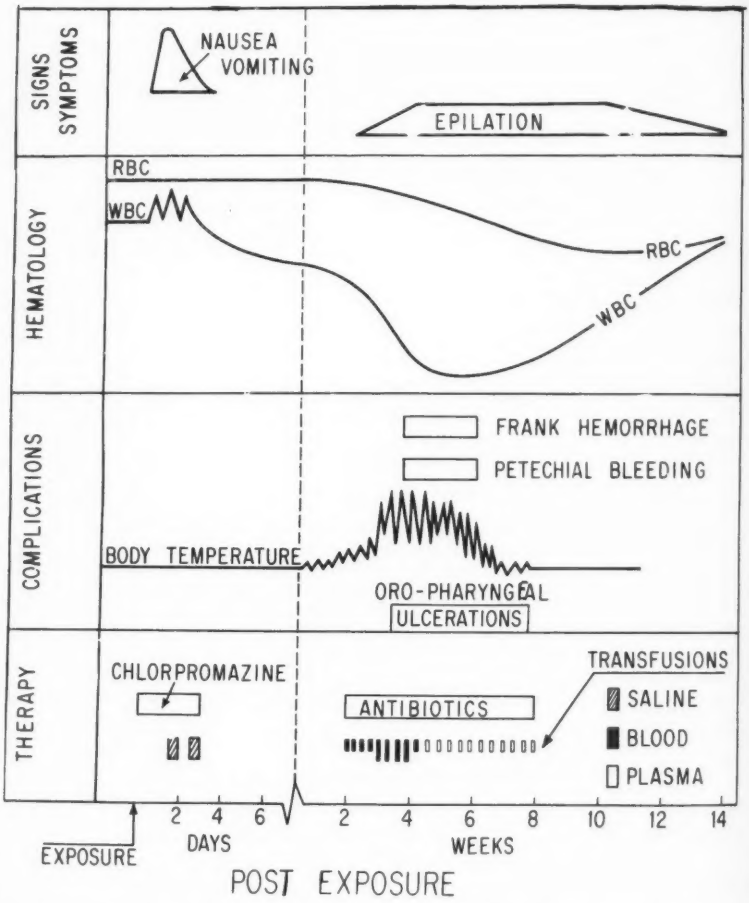

Figure 8. Schematic drawing showing the temporal relationship between clinical course and therapeutic management of the hematopoietic form of the acute radiation syndrome.

will soon be possible as a result of current research efforts—injection of bone marrow or spleen material, controlled cross-transfusion with healthy donors, and isolation of bone marrow-stimulating substances.

Under the catastrophic conditions prevailing in Hiroshima and Nagasaki, the mortality of the fully developed hematopoietic

form was 50 per cent. Among those patients who were treated at reasonably well equipped hospitals in Tokyo, the corresponding mortality was 30 per cent. With modern facilities, with sufficient types and amounts of antibiotics, and with the rapidly advancing technics for the transfusion or exchange of fresh whole blood or any desired constituent of it, a much lower mortality rate can be achieved.

A discussion of some additional medical problems posed by nuclear disasters is contained in references 53 and 54.

CONCLUSIONS

Since penetrating ionizing radiation has all the potentialities of becoming a major casualty-causing agent, the peculiar clinical picture caused by this new type of injurious factor must be understood. Only knowledge can help to dispel the many uncertainties and misconceptions surrounding the radiation problem. Exposure of the whole body, or of a large part of it, to sufficient amounts of penetrating ionizing radiation induces in man the acute radiation syndrome. Clinical course and outcome of the disease are determined, in essence, by two factors—dose and individual susceptibility. At present, the factual evidence is not strong enough to establish with high accuracy the interplay between these factors in an exposed population. Since, therefore, most of the figures concerning incidence and severity of radiation-induced injury must be based largely on extrapolations and estimations, their value is necessarily provisional and subject to revision when additional information becomes available. Nevertheless, the following broad statements seem to be rather well supported by data originating from radiotherapy, nuclear accidents, and atomic bomb explosions: Air doses up to 100 r will be subthreshold for the acute radiation syndrome, and will thus be of no concern in emergency situations. In the dose range between 100 and 200 r, the acute radiation syndrome, if it develops at all, will proceed in such a mild form that it can be handled ambulatorily. The *hospitalization threshold,* a very important concept defined as that dose level beyond which hospitalization becomes necessary for an appreciable number of persons among a large exposed population, lies approximately at 200 r. Between 200 and 400 r—perhaps even 500 r—the acute radiation syndrome will be clinically significant and will occur in its hematopoietic form, displaying a very characteristic time course almost independent of dose. Knowledge of this time course should help in the advance preparation for medical personnel, supplies, and housing facilities. With these steps taken and under proper therapeutic management, the radiation-induced disease will have a favorable outcome in the overwhelming majority of cases. All facts available disprove the fatalistic or pessimistic approach frequently encountered. In emergency situations

this dose range represents a great and rewarding challenge to the physician. Very little is known about doses above 500 r. Here, most likely, a fulminating clinical course with gastrointestinal involvement will prevail, and the outcome is at least dubious. Presently available facts are insufficient to either support or contradict the assumption that an acute exposure to 600 r is the highest one compatible with human survival.

The conclusion is that in a wide dose range man can overcome the acute radiation syndrome and return to a useful life. There exists no account of the many thousand survivors of Hiroshima and Nagasaki who resumed their previous occupation with full vigor, while there are several reports relating each case of leukemia, cataract, or neoplasm. Understandably, as any other severe disease, the acute radiation syndrome may be followed by late complications in a relatively small percentage of cases. Further observations must be made before an unbiased judgment is possible about incidence and importance of late consequences of irradiation.

SUMMARY

From a comparative analysis of human data derived from nuclear accidents, Japanese bomb casualties, and radiotherapy patients, emerges the clinical picture of the acute radiation syndrome with its three subdivisions—hematopoietic, gastrointestinal, and cerebral forms. Dependency of the picture on dose level and individual susceptibility is discussed, and the therapeutic management is outlined. Since penetrating ionizing radiation represents a potential casualty-causing agent, problems facing the practical physician under catastrophic conditions are evaluated.

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CARE OF THE PATIENT WITH BLOOD VESSEL INJURY

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ADVANCES in the field of vascular surgery have resulted in a significant reduction in the amputation of limbs following trauma. The military medical services have contributed substantially to these advances as evidenced in the recent Korean conflict.[1-8] Inasmuch as vascular surgery is a relatively new field, this subject is presented further to familiarize the military medical officer with the care of the patient with major blood vessel injuries.

Few patients with injury to the major vessels of the abdominal and thoracic cavities live to reach a hospital; therefore, most surgery of acute vascular injuries involves the peripheral vessels, but injuries to these vessels require prompt surgical attention. Because vascular surgery is urgent surgery, it is most important that every surgeon confronted with the care of patients with acute vascular injuries constantly keep in mind the basic principles of management of the wounded. Patients with major blood vessel damage are usually in poor condition. It is essential, therefore, that they be properly resuscitated and evaluated for priority of care of all injuries and for ability to tolerate any additional time required for vascular surgery. Failure to observe these basic principles may result in a loss of life in an attempt to save a limb.

PREOPERATIVE CARE

Vascular injuries may be presented as open wounds, varying from minor lacerations to avulsions, or as occlusions resulting from spasm, emboli, displaced bone fragments, or other complications of trauma. A differential diagnosis may be difficult, but, when in doubt, the patient should be treated as having a vascular injury. A cold, pulseless limb may result from exposure, shock, spasm, compression, or from arterial injury. External hemorrhage may or may not be present. An accurate diagnosis often cannot be made until wound debridement, although a wound in the vicinity of a large vessel should arouse suspicion of vascular injury.

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Comparison of pulses, color, and skin temperature in the two extremities should be helpful in making a diagnosis. Regardless of the type of injury, the objective of treatment is restoration of arterial blood flow at the earliest possible moment.

Definitive surgery may not be feasible in the area of initial care. However, the diagnosis should be made, preliminary management begun, and plans made for emergency evacuation. When the situation dictates transfer of the patient, evacuation should be facilitated as soon as the condition permits. During resuscitation it is preferable to replace tourniquets with pressure dressings for the control of hemorrhage. In rare instances a tourniquet may be required, but most pressure dressings applied with an elastic bandage can be applied as tightly as a tourniquet, if necessary. In wounds exposing the damaged vessel, clamps may be applied to the open ends of the vessel for control.

OPERATIVE CARE

After arrival of the patient at an installation where vascular surgery is available, under anesthesia, the operative site is prepared by shaving and scrubbing and the wound is irrigated with sterile saline solution. The presence of a pneumatic tourniquet for use at surgery is desirable whenever applicable, but should be left uninflated except when actually required. In large wounds the ends of the vessels may be visible and controlled directly, otherwise an anatomic approach to the injured vessel is used, regardless of the wound location. The artery is approached first proximal then distal to the site of damage, control tapes are placed about the vessel, and dissection is carried toward the point of arterial injury. After the artery is controlled, attention then is given to debridement of the wound, which must be débrided thoroughly and irrigated as in any traumatic wound.

The vessel must be examined to determine if there is more than one site of injury. Vessel wounds created by tiny missiles may appear benign, but on closer examination the small area of trauma may be found to extend for some distance. Small wounds often are plugged by a clot which extends into the lumen, masking the injurv and serving as a focus for thrombosis or embolism. Frequently, missiles also perforate the opposite wall. Such wounds, if not properly treated, may result in secondary hemorrhage, occlusion of the artery, or the development of a false aneurysm.

The treatment of an arterial injury resolves itself into three categories: (1) repair, (2) ligation, and (3) conservative or nonoperative management with delayed definitive care.

Repair. An artery partially lacerated by a sharp instrument with negligible contusion may be sutured simply with minimal debridement. The more severely lacerated or severed vessel must be debrided in accordance with the surgeon's best judgment. Repair

is preferably by anastomosis when possible (fig. 1), and the majority of repairs can be accomplished in this manner. In general up to 2 cm of vessel can be sacrificed and still permit anastomosis. Judgment as to the amount of tension that an anastomosis will stand comes only with practice. When repair by anastomosis is

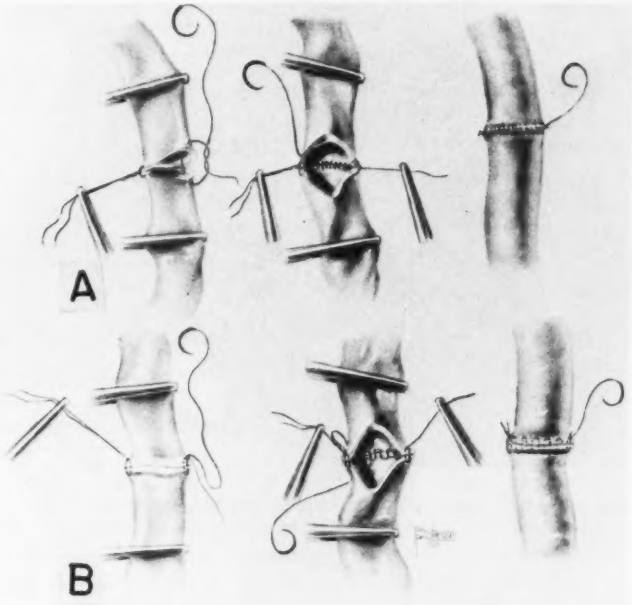

Figure 1. A *demonstrates the steps of anastomosing a vessel, using a continuous over-and-over suture.* B *demonstrates the use of a continuous transverse mattress suture, for comparison with the simple suture method shown in* A.

not possible without undue tension, a graft must be inserted. A homologous artery graft or an autogenous vein graft (fig. 2) may be used. Veins accompanying the artery are usually too large for use and, furthermore, should not be sacrificed but should be preserved whenever possible.

After arterial repair it is imperative that the vessels be covered for nourishment and protection from infection. Viable muscle and subcutaneous tissue are satisfactory, while fascia, because of its poor vascularity, is not. Furthermore, the site of vascular suture must not be wrapped in some impervious foreign material which prevents revascularization. Coverage of the vessels does not imply closure of the wound.

Care also must be taken to protect suture lines at joint sites. Such extremities usually are fixed in 15° to 20° flexion following

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repair, to reduce tension at the suture line. During the healing period the extremity must be taped or splinted to prevent violent extension with separation of the suture line. The same care must be exercised with patients having vascular repairs in the presence of fractures. Excessive traction may result in rupture of the suture.

Figure 2. A saphenous vein graft which has been reversed and sutured into the defect in the brachial artery following an acute injury.

line, or displacement of the bone fragments may lacerate or compress the repaired vessel. A well-padded basket or splint should be used to hold the fracture in position. Undue constriction and pressure from casts must be avoided for 10 to 15 days, until healing of the vessel has occurred.

Ligation. There are indications for ligation of major vessels. This procedure may become necessary when the condition of the patient will not permit the additional time required for surgical repair. In large avulsed wounds where coverage of vascular grafts is impossible, ligation also may be utilized. When evacuation to a center equipped for vascular repair is impossible, then ligation of the vessels should be performed rather than leave a tourniquet in place and delay débridement indefinitely. Even if facilities are present, ligation may be necessary because of the large volume of cases and inability to spare time for limbsaving at the expense of livesaving. With ligation procedures one may expect an over-all incidence of gangrene in approximately 50 per cent of the limbs where major vessels are ligated. The incidence of gangrene varies from 70 to 100 per cent for the more critical arteries such as the popliteal, to from 25 to 30 per cent from

ligation of the brachial artery below the profunda. Elective ligation of the concomitant or companion vein at the time of ligation of the artery is contraindicated. Ligation of minor arteries such as the profunda in the arm and thigh, or one of the small arteries in the forearm or leg, does not endanger survival of the extremity. Even though ligation of a vessel may not result in gangrene, it frequently results in arterial insufficiency.

Conservative Treatment. An artery may be partially severed with little or no evidence of external hemorrhage but develop a pulsating hematoma. When both artery and vein are injured, an arteriovenous fistula may be formed, with flow of blood directly from the artery to the vein. Patients with such injuries, with controlled hemorrhage and viable extremities evidenced by distal palpable pulses, should be given a lower priority for surgery. Conservative care is particularly applicable to wounds of the carotid and subclavian arteries with controlled pulsating hematomas.

Patients treated conservatively should have minimal wound débridement with care taken not to dislodge the clot and to avoid wound infection. Careful observation is necessary for expansion of the hematoma with compression of vital structures (fig. 3), hemorrhage, or infection.

COMPLICATIONS

While there is no great mystery surrounding vascular surgery, there are a number of seemingly minor but important details which contribute to successful blood vessel repair with minimum complications. Lack of facilities is certainly an indication for prompt evacuation as soon as the patient is in condition to travel. Although a competent surgeon may be present, necessary instruments may be lacking. The reverse situation—with proper instruments available to the untrained surgeon—may be more disastrous. It is extremely beneficial to have developed technic in an experimental laboratory, or to have assisted with vascular surgery prior to operating on one's first patient. Attempts of the surgeon inexperienced in vascular surgery to repair blood vessel injuries have resulted in tragedy. Loss of the patient's life is likely to be the result of the eager surgeon who fails to evaluate properly and resuscitate the patient before rushing him to the operating room in an attempt to save a limb. The same disaster may occur from unwisely prolonging surgical intervention by the additional time required to perform blood vessel repair following other major abdominal and thoracic surgical procedures. Lives also have been lost from opening a pulsating hematoma without adequate proximal and distal control of the vessels entering the hematoma. Limbs have been lost by the inexperienced surgeon who has opened pulsating hematomas and found, to his despair, that he could not repair the arterial damage. Limb loss also has resulted from

attempted repairs in which collateral branches were sacrificed to permit anastomosis of the vessel, only to have the anastomosis fail from constriction, spasm, or thrombosis.

Figure 3. A pulsating hematoma is demonstrated in the popliteal space. While the hematoma is self-contained and the extremity is viable, swelling of the leg is evident. Because of the tight popliteal space, expansion of the hematoma in this area can result in early nerve damage or ischemia to the leg.

The most important cause of limb loss is time lag from injury to arterial repair. Best results are obtained in those patients having repair within 10 hours of injury. This does not mean that there should be a time limit beyond which an arterial repair should not be done. There are many variables that make it impossible to set a time limit for repair. Because it is not always possible to judge clinically the irreversibility of ischemic muscle, it is good practice to repair major blood vessel injuries even when in doubt of irreversibility of damage. With restoration of the blood supply to muscles of questionable viability the patient must be observed for evidence of acute renal failure. Evidence of renal involvement with decreased urinary output and increased serum potassium and nonprotein nitrogen levels may be an indication for early amputation of the nonviable limb or excision of necrotic tissue.

Frequently, the ischemic limb exhibits a contracture resembling Volkmann's contracture. This may be reversible if the blood supply

is restored in time. Upon restoration of blood flow to such limbs, the muscles tend to develop edema as a result of the ischemic changes, and, if fasciotomy is not performed, the continued volume increase of the muscle within the closed fascial compartment results in the compression of vessels, nerve damage, and necrosis of tissues. Failure to recognize this process has resulted in permanent nerve damage and loss of compartments of muscles and extremities following an otherwise satisfactory vascular repair (fig. 4).

Figure 4. Here the late results of Volkmann's contracture and ischemic swelling are noted. Admitted with axillary artery and upper arm injuries, the limb muscles were ischemic and contracted. Following repair of the axillary artery, swelling of the forearm occurred, and fasciotomy was performed too late to preserve the flexor muscles.

When segmental spasm occurs following arterial injury, it often can be treated successfully by the use of 2.5 per cent papaverine hydrochloride[6] or 1 per cent procaine hydrochloride applied locally to the spastic segment. Generalized spasm of the arterial tree may be improved by sympathetic block with 1 per cent procaine hydrochloride, or spinal or caudal anesthetic block may be given as a single or as an intermittent or continuous application, as indicated.

Anticoagulants are not indicated in these cases and may lead to serious hemorrhage, particularly in the patient with multiple injuries. The complications of hemorrhage from the vascular repair should not be a problem if the vessel has been properly debrided, properly sutured without undue tension, and properly covered and

protected from abnormal stress at joint and fracture sites. Infection that also will cause hemorrhage or thrombosis should not be a complicating factor if the wound has been properly debrided and cleansed. In order to ensure further against infection, antibiotics may be given for approximately five days, but antibiotics should not be used as a substitute for good surgery. There is no substitute for careful resuscitation and evaluation of the injured patient before surgery.

SUMMARY

The essentials of care of the patient with blood vessel injury are presented in order better to acquaint military surgeons with accepted concepts. As always in trauma cases, assessment of the total injury, resuscitation and adherence to priorities in treatment are of extreme importance, often making the difference between life and death and saving or losing a limb. Treatment of arterial injury falls into three categories: (1) repair, (2) ligation, and (3) nonoperative management with delayed definitive care. Specific indications for each exist. Judgment as to what to do and when to do it, coupled with technical skill developed before the emergency arises, will save limbs and lives. Improper hemostasis, lack of technical training, and poor judgment result in loss of life and limb.

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FIVE- TO NINE-YEAR FOLLOW-UP OF PULMONARY RESECTIONS FOR TUBERCULOSIS

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THE PURPOSE of this paper is to report a five- to nine-year study of 59 consecutive patients with pulmonary tuberculosis who had their major foci of disease removed by segmental and subsegmental resection during the period January 1948 to September 1952. Local enucleations of superficial lesions are not included.

In 1953 Chamberlain and associates[1] reported on 300 similar cases followed for from one to five years. They described the indications for surgery and the operative and postoperative management to which we have adhered at this hospital. Both the technics and the management used in our cases were those developed by Chamberlain.[2,3]

In the present era of antituberculosis drugs, segmental resection has become well established both here and abroad as a reasonably safe method by which the tuberculous patient may be separated from his caseous, fibrocaseous, and cavitary, residual, necrotic foci.[4-7] Most of the patients reported on in this paper, however, had their resections prior to the current "drug era." Many of them were inadequately covered by drugs at the time of operation; many were re-treatment cases; and others had had previous surgical maneuvers to control their disease.

Since 1952 there has been more uniformity of treatment. The majority of the patients now come to the surgeon having had at least six months of drug therapy as a "first course," without prior surgical intervention, and with negative sputums. Because of these advances, as well as better selection of patients for segmental resections, the more recent results have shown marked improvement. There have been no surgical deaths and only two

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serious complications in our last 146 patients operated on for tuberculosis by this technic.

The average age of the patients in the present study was 33 years, the youngest being 19 and the oldest 56. Four of the 59 patients are dead and 55 are living. Of the living, 53 are well and capable of working; 1 had a recent reactivation that at present is under control by drugs; and 1 is untraced, although known to be alive. There is thus a 98.3 per cent follow-up.

The mortality in this series has been 6.8 per cent over a five- to nine-year period. In only one of the four cases where death has occurred was the cause of death directly related to tuberculosis. The immediate operative mortality was 1.7 per cent; the total, 3.4 per cent. One patient had a postoperative hemorrhage, with acute tubular necrosis and death in uremia. Another patient, after multiple operations, required pneumonectomy to control a bronchopulmonary fistula with empyema, and died from an anesthetic accident 20 minutes after the operation. The remaining two patients each lived for four years postoperatively and died of coronary occlusion.

The location of the tuberculous foci is shown in table 1. There was a predominance of left-sided disease in this series. This was particularly evident in regard to apicoposterior resections, of which there were 22 on the left but only 13 on the right. The small size of the series makes this perhaps more interesting than significant. Examination of the pathologic reports of the resected specimens revealed that there were 15 patients with cavities as the predominant lesion, 40 with fibrocaseous involvement, and 4 with tuberculous granulomata.

TABLE 1. *Location of tuberculous foci in 59 patients*

	Right	Left	Total
Segments	35	52	87
Subsegments	7	10	17
Total	42	62	104

In 13 patients, there were early complications. These are listed in table 2, together with the operation performed, the result of a sputum examination at the time of operation, the treatment of the complication, and the present status. It has been stated[1] that the degree of activity of the disease at the time of operation does not influence the complication rate. In this series it may be significant that the sputum was positive in each of the four

TABLE 2. *Early complications seen in 13 of 59 patients*

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Case	Segmental resection performed	Sputum at operation	Complication	Treatment	Present status
1	AP, LUL	Positive	Space	Thoracoplasty	Well
2	ANT. & AP, RUL	Positive	Space	Thoracoplasty	Dead; coronary occlusion
3	AP, RUL	Positive	BP fistula & empyema	Thoracoplasty & pneumonectomy	Dead; anesthetic accident
4	AP, LUL	Positive	Space	Thoracoplasty	Well
5	AP, LUL	Positive	Space	Phrenic crush	Well
6	AP, RUL	Negative	Space	Thoracoplasty & decortication	Controlled under 2nd Rx course
7	RML	Negative	Space	Thoracoplasty	Well
8	AP, RUL	Negative	Hemorrhage	Thoracotomy	Dead; acute labular necrosis
9	ANT. RUL	Negative	Space & positive culture	Refused operation	Well after homolat. spread
10	SS, LLL	Positive	BP fistula	Thoracoplasty & myoplasty	Untraced (living)
11	AP, LUL	Negative	Space	Pneumoperitoneum & phrenic crush Refused thoracoplasty	Recently stable
12	AP, LUL SS, LLL	Positive	BP fistula	Thoracoplasty	Well
13	AP, RUL	Positive	BP fistula	Closure of fistula & thoracoplasty	Well

AP: apicoposterior
LUL: left upper lobe (et cetera)
BP: bronchopleural
SS: superior segment

patients who developed bronchopleural fistulas, and that those with negative sputums who developed some complication other than fistula also demonstrated poor resistance to tuberculosis by having eventual reactivation.

Table 3 presents the approximate percentages of bronchopleural fistula and the early (operative) mortalities in other recently published series of segmental resections for tuberculosis. Because the method of case analysis varies with each paper, some of these figures are ours, derived by us from the material as presented.

TABLE 3. *Percentages of operative deaths and of occurrence of bronchopulmonary fistula in series of segmental resections for tuberculosis reported by various authors*

Authors	Cases	Operative mortality	Bronchopulmonary fistula*
	Number	Per cent	Per cent
Thompson, Savage, & Rosser[6]	63	3	4.7
Efskind, Fretheim, & Vaksvik[7]	82	3.6	
Cole & Alley[13]	61		9.1
Bickford & associates[4]	75	1	
Pacheco & associates[10]	45		9.3
Chamberlain & associates[1]	300	1	5.3
Chamberlain[3]	161	2	6
Thomas[8]	58		3.4
Gale & associates[9]	434	0.5	3 (over-all)
Perry & associates[14]	105	3.1	12 (mental patients)
Hering & Timmes	59	1.7	6.8

*Large bronchial leaks requiring definitive surgery, rather than alveolar leaks presenting only temporary space problems.

In 5 of the 59 cases in this series, there was reactivation of tuberculosis at some time subsequent to the segmental resection. One 26-year-old man had a preliminary contralateral thoracoplasty in 1948 and a segmental resection in September 1949. He had a contralateral reactivation in 1953, but following revision of the thoracoplasty is now well. A 56-year-old man with positive sputum at time of operation in May 1949 had an ipsilateral reactivation in 1951. He was retreated and stabilized, but died of coronary occlusion 13 months later. A man who had an apical segmental resection in March 1951 suffered ipsilateral reactivation in the posterior segment the same year. Following a second resection, he has remained well. A 25-year-old man had a space problem

following operation in March 1951. Contralateral reactivation was stabilized by a second course of drugs, and he is now well. A 20-year-old man had a persistent space after resection of the anterior segment, right upper lung, in October 1951. He developed a positive culture three months after the operation, and an ipsilateral upper lobe cavity within a year. Following a second course of drugs in 1953, he is now working, with inactive disease.

DISCUSSION

The chief value of this paper derives from the long follow-up of consecutive patients who were operated upon in the 1948 to 1952 era. Although the results obtained in this series compare favorably with other similar series of segmental resections, future reports should show improvement in the rates of complications and mortality because of: (1) preoperative drug schedules which are more uniform and effective; (2) proper selection of patients at the operating table for the segmental type of operation; (3) a larger percentage of primary treatment cases and cases without such extensive disease as was seen formerly; and (4) greater familiarity of the surgeon with the strategic maneuvers attendant upon postoperative care.

Certain technical refinements in current use, not necessarily original with us, include the following; (1) early division of the bronchi; (2) use of extrapleural dissection in the cupola of the chest to facilitate the handling of dense, vascular adhesions; (3) occasional construction of an apical pleural tent in the hope of preventing intrapleural space problems; and (4) suturing of the segment or segments remaining, to the adjacent lobes in such a manner as to prevent torsion, and where possible, to cover the raw surfaces.

Some authors have mentioned placing streptomycin sulfate and penicillin in the pleural cavity, the use of one lower tube, and gentle postoperative suction.[9] We have preferred not to use intrapleural drugs, have used two tubes, and as much suction as is necessary to stay ahead of leaks. Gale and co-workers[9] warned against the use of strong suction in the presence of atelectasis and air leaks. Pacheco and associates[10] believed that the incidence of fistulas is related to the "existence of a residual pleural cavity."

Bickford and associates[4] preferred immediate thoracoplasty if more lung volume than two segments is removed. We have not followed any rule, preferring to assess each case at the operating table in the light of estimated lung-thorax compliance. Bell[11] reminded us that thoracoplasty should be done early enough in the control of postoperative complications to preclude the development of rigid walls. He also pointed out that many postoperative

spaces are negative or neutral in pressure, and may respond to conservative measures. Wareham and co-workers[12] listed certain criteria for the conservative management of postoperative spaces: (1) absence of symptoms; (2) progressive shrinkage of the space (using tomograms); (3) negative sputa; and (4) effective antibiotics.

Each of the foregoing factors merits careful consideration, with individual assessment of each patient. Assiduous attention to operative and postoperative detail is of vital importance, and, as Thomas[6] mentions, this will keep errors related to the human factor at a minimum.

SUMMARY AND CONCLUSIONS

Fifty-nine consecutive cases operated upon by segmental resection for tuberculosis five to nine years prior to September 1957 are presented, with a 98.3 per cent follow-up. Of 55 who are living, 53 are well enough to work, 1 is living with recently arrested disease, and 1 is untraced, although known to be alive. Four are dead, two of unrelated causes, one an operative mortality, the other because of an anesthetic accident following successive operations for persistent tuberculosis. The operative mortality was 1.7 per cent and the incidence of serious bronchopleural fistulas, 6.8 per cent. Reactivations of the disease were five in number, three homolateral and two contralateral. All were controlled.

Certain aspects of the surgical treatment of pulmonary tuberculosis are discussed, with references to recent, similar series of segmental resections. It is concluded that this procedure, as demonstrated by long-term follow-up, is a safe and effective method of treating tuberculosis. Even *without* our present-day use of adequate drug therapy, segmental resection proved to be an effective method of treatment. With modern drug coverage, it has been demonstrated to be safer, and should prove to be still more effective.

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RECREATIONAL THERAPY IN PSYCHIATRY

"Dr. Hack Tuke, who is to my mind one of the most neglected of the psychiatric classicists and who, with Pinel, was perhaps the most significant psychiatrist of the early 19th Century,... had noted at his private sanitarium, The York Retreat, an interesting and for that period a remarkable observation, namely, that psychiatric illness did not seem to so largely affect members of the artisan class.... Only 50 years earlier Europe had been astounded to learn that King Louis XVI of France found it relaxing to employ as a hobby the trade of a locksmith which he had learned from a servant as a boy, and we read that he passed the long months in prison prior to his execution by repairing locks. Tuke, who discovered this, took this lesson to heart and despite the resistance of both his patients and the medical profession, organized a series of little craft shops in The York Retreat and was the first to describe the beneficial results which accrued to patients by work of this nature. He gradually came to learn, as we now know so well, that all work and activity in the hospital may have a therapeutic as well as an educational value for the persons who undertake it."

—C. W. WAHL, M. D.
in *American Journal of Occupational Therapy*
p. 278, Sept.-Oct. 1957

REQUIREMENT FOR REDUCTION IN ANTIBIOTIC DOSES DURING OLIGURIA

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ROBERT B. W. SMITH, *Major, MC, USAF*

IT IS well established that many antibiotics are excreted principally in the urine, and that the size and frequency of antibiotic doses should be reduced during renal insufficiency.[1] In spite of this information, many physicians continue to prescribe antibiotics according to rules of thumb, without regard for diminished excretion during oliguria. In addition, some texts on the management of renal insufficiency either neglect to mention this important point or advise "antibiotics in full doses" for pyelonephritis with oliguria, which cannot always be distinguished from nonbacterial renal disease. As a result, a high proportion of the patients with oliguria (less than 500 ml of dilute urine per 24 hours) arriving at this hospital have exceedingly high blood concentrations of antibiotics. The toxicities of antibiotics are familiar to all and will not be reviewed here. The purpose of this report is to document the adequacy of small, infrequent doses and to re-emphasize the need for a flexible regimen.

METHODS

The streptomycin and tetracycline assays were performed by the streptomycin method of Romansky and Bedsole,[2] and the penicillin and erythromycin assays by the serial-dilution tube technic of Rammelkamp,[3] both modified to give a maximum reading of 100 μg or units per ml.

CLINICAL MATERIAL AND RESULTS

Random analyses for antibiotic concentrations in the blood of 12 oliguric patients revealed values in excess of 100 μg of streptomycin per ml in 4 patients, 100 units of penicillin per ml in 7 patients, 150 μg of erythromycin per ml in 3 patients, 67 μg of tetracycline per ml in 3 patients, and lesser but still excessive concentrations of these and other antibiotics in several additional patients. The administration of antibiotics, where recorded, had

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been in the range usually employed in patients with normal renal function. In general, the blood concentration of streptomycin exceeded the therapeutic range by a greater percentage than that of other antibiotics also administered in standard doses. Because of this observation and the more serious toxicity of streptomycin, it was selected for further examination in oliguric patients.

The blood concentration of streptomycin was assayed in 10 oliguric patients who had been receiving streptomycin prior to admission. Although the previous dosage schedule was not surely known in all instances, several patients had no record of having received any antibiotic during the preceding day or two, when they were in transit from an overseas hospital. In 8 of the 10 patients, blood was drawn on admission for the initial determination, after which 0.5 gram streptomycin was administered to each patient. The blood concentration of streptomycin was first determined on the remaining two patients on the day after admission. During the next few days no antibiotic was given to any of the 10 patients, and the blood concentrations were assayed repeatedly.

As shown in figure 1, seven of the eight patients examined on admission already had blood levels in or above the therapeutic

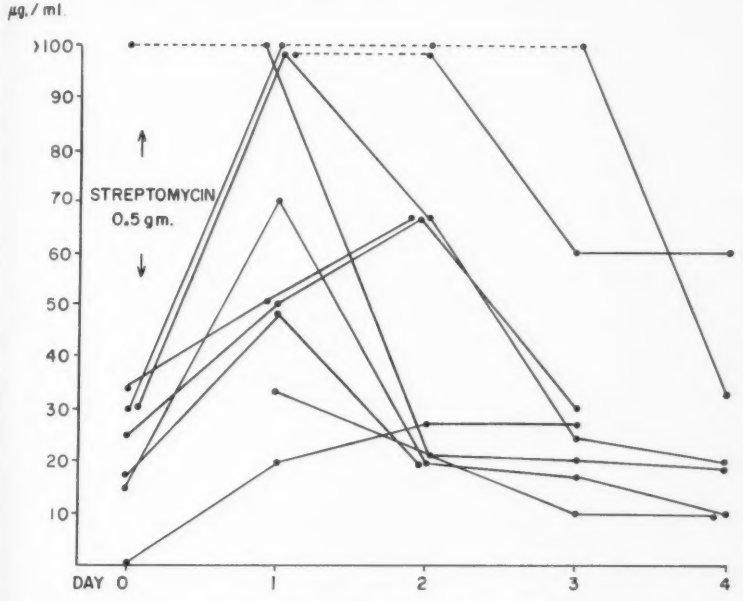

Figure 1. Streptomycin concentration in the blood of 10 oliguric patients. After blood for assay was drawn from 8 of the patients on day zero, each of the 8 patients received 0.5 gram of streptomycin. No antibiotic was given to any of the 10 during the next 4 days.

range, before the 0.5-gram dose was given. One day later most of the blood levels were well into the range usually considered to be toxic. The only patient who had a blood level that probably is satisfactory, 20-27 μg per ml, was the one who had had no detectable streptomycin in his blood before receiving the 0.5-gram dose. The patient with the next lowest blood level on the first day, 33 μg per ml, was not examined on admission, but presumably had a low level.

The time required for the blood levels to fall varied, and could not be evaluated completely because in some patients the period of observation was interrupted by artificial hemodialysis, which removes streptomycin from the blood. One patient, however, still had 60 μg per ml four days after the last dose was received, and none of the six patients examined at that time had values under 10 μg per ml.

One patient, to be described in detail in a subsequent report, was oliguric for 97 days, presenting an opportunity to observe the effects of the same dose of streptomycin given at varying intervals. As shown in figure 2, 0.5 gram streptomycin was excessive as a maintenance dose. When given at a time that the blood level was already in or above the therapeutic range, it drove the concentration to toxic levels. The only time the rise was limited to the high therapeutic range (25 μg per ml) was the one

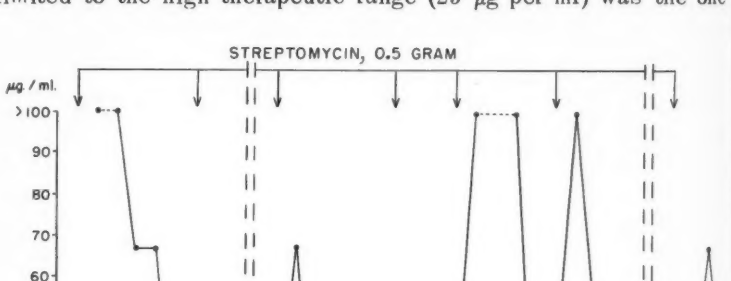

Figure 2. Streptomycin concentration in the blood of a patient with prolonged oliguria. Streptomycin, 0.5 gram, was given at varying intervals of several days, indicated by the arrows.

occasion on 19 September when the preinjection level was rather low (2.5 μg per ml), six days after the last dose. On another occasion, on 2 September, a therapeutic concentration was still present after six days, the preceding levels have been extremely high.

These data demonstrate that even so modest a dose as 0.5 gram of streptomycin is adequate to raise the blood level from essentially zero to a therapeutic range. It is presumed but was not demonstrated that the same magnitude of increase would occur in a patient who had not previously received the drug. Certainly 0.5 gram is too large a dose to give if an adequate concentration is already present. Although the data are not adequate to establish exactly the amount or frequency of dosage required to attain and maintain but not to exceed a therapeutic level, they indicate that an initial dose of 0.5 gram and maintenance doses of 0.25 gram every two or three days would be reasonable.

It is not possible to state whether or not the extremely high levels produced ill effects. Most of the patients had bizarre symptoms at some time during their course, but because the symptoms of uremia are variable and unexplained, any specific effects of streptomycin could not be judged. It has been observed, however, that massive doses of certain antibiotics to nonuremic patients, which might correspond to small doses to uremic patients, have produced serious symptoms reminiscent of the manifestations of uremia alone.[4] The present observations were based on an antibiotic assay of streptomycin and took no account of the unexcreted degradation products, which, though lacking antibiotic activity, could have serious biologic effects.

Without implying further that such extreme blood concentrations are significantly harmful, it can be stated without reservation that they are not desirable.

SUMMARY

In oliguric patients, small doses of antibiotics may produce excessive concentrations in the blood, because the principal route for excretion of many antibiotics is the urine. The finding of extremely high concentrations of several antibiotics at the time of admission of patients with oliguria prompted a study of the blood levels of streptomycin for several days after a single dose of 0.5 gram. This dose proved excessive for patients who already had a significant blood level, but probably is optimal as an initial dose. Maintenance doses of 0.25 gram at two- or three-day intervals appear reasonable.

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SALICYLATES AS A CAUSE OF GASTRIC HEMORRHAGE

"...Salicylates may cause bleeding from the gastro-intestinal tract by several mechanisms, operating either singly or in combination. These are by the production of hypoprothrombinaemia, by local tissue irritation, by gastric allergy, by an increase in gastric acidity, and by an effect on the gastric mucous cells or on mucin itself. The administration of salicylates appears to increase the frequency of bleeding in patients with proven peptic ulcers, but apart from this it is clear that a small group of subjects are much more susceptible than others.... An observed seasonal incidence of peptic ulcer activation may be partially explained by the more frequent use of aspirin in the 'ulcer months,' which coincide with the peak period for upper respiratory tract infections and minor illnesses, such as the familiar "flu," for which the usual treatment is aspirin with rest.

"...All patients who suffer from upper gastro-intestinal hemorrhage should be questioned concerning the use of salicylates or proprietary drugs containing salicylates. This needs to be done with care, as aspirin is an almost universal form of self-medication, and many people would fail to think of it as a 'drug.' A little trouble taken in clearing up this point may spare a patient future episodes of bleeding, needless operation (for subtotal gastrectomy has been carried out for bleeding probably due to aspirin ingestion), and perhaps even his life."

—EDITORIAL
in *Medical Journal of Australia*
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REPAIR OF CRANIAL DEFECTS WITH ANTERIOR ILIAC BONE GRAFTS

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A PROBLEM confronting surgeons at an overseas center is the return of all salvageable patients to active duty. Patients with large cranial defects following depressed skull fractures, especially those involving the frontal sinuses, previously were evacuated to the United States from our hospital. The danger of secondary infection in such wounds was considered so great that early cranioplasties employing the inert metals or plastic resins were not performed.

The early repair of very large cranial defects with autogenous bone was considered more feasible because of the reduced incidence of infection with such grafts. The difficulty in obtaining the graft, the size and shape of a readily obtainable graft, and the added risk and discomfort to the patient were evaluated for the usual donor sites—tibia, rib, ilium, et cetera. One of us (T. H. C.)[1] previously had taken a large number of grafts from the anterior crest of the ilium for other purposes. The procedure was simple and did not cause serious discomfort or ensuing debility. Furthermore, the shape of a split-thickness anterior iliac graft corresponded to the contour of the skull, and large grafts were readily available.

The following report concerns an initial study of 12 cranioplasties accomplished with autogenous split-thickness grafts from the anterior crest of the ilium.

METHOD

The use of iliac bone as an autogenous source for bone-grafting procedures has been increasingly popular. This popularity is justified because of the ready availability of a generous amount of bone, the general lack of complications following the removal of graft from the donor site, and the rapidity with which the cancellous bone from the ilium usually unites with the recipient bed.

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In this series, it has been our practice to take a split-thickness graft, resecting and using only the outer cortex of the anterior portion of the ilium. This has provided a generous source of bone in one solid sheet, which, with its natural smooth concave cortical surface, has been found to fit accurately against the dura mater, leaving the cancellous surface in juxtaposition to the rich blood supply of the scalp. Furthermore, by leaving one cortex of the ilium intact, the contour of the pelvic girdle is undisturbed and no appreciable structural defect is produced nor is muscular strength of the leg and thigh impaired.

Because cranioplasty is an elective procedure, the technic of securing the graft is preceded by 24-hour preparation, during which the pubic area and donor site are shaved and scrubbed with pHisoHex (brand of hexachlorophene) and then covered with sterile dressings. In the operating room, the skin is scrubbed again with pHisoHex and draped in the usual sterile manner.

The incision is started at the anterosuperior crest of the ilium and directed backward along the crest for the required size of graft needed. The incision is carried through the periosteum longitudinally at the mid-portion of the crest, at about the junction of the attachments of the abdominal and gluteal muscles. The periosteum, with the origin of the gluteal muscles, is then stripped from the lateral cortex of the ilium, using a periosteal elevator or a bone chisel where the strong, fibrous attachments require a sharp dissection. Usually it is not necessary to detach the attachment of the tensor fasciae latae, the sartorius, or the inguinal ligament from the anterior superior iliac spine, as this projection of the bone seldom is required in the pattern of the defect. Their strength can thus be unimpaired, though it certainly is permissible to use this portion of the bone, if needed. In such case one should be careful to avoid the lateral femoral cutaneous nerve. Cutting this will cause bothersome anesthesia of the thigh and, on occasion, painful neuromas.

The bone is secured best by using a cloth pattern taken from the cranial defect prior to surgery and sterilized so that it can be placed against the outer cortex of the ilium as a guide. The pattern can be outlined by incising the cortex with a sharp osteotome, and the graft removed by splitting the ilium sagittally from the crest with a broad-blade osteotome. In young patients who have not yet completed their growth, the epiphysis is left undisturbed and the graft resected from an area at least 1 cm proximal to the epiphyseal line. The cut edges of the ilium are impacted, and the gluteal muscles are reattached to the periosteum at the remaining crest of the ilium. These muscles act as a tampon, and to a large degree prohibit bleeding from the raw bone. It is advisable, however, to insert a rubber drain down to the bone from the posterior extremity of the wound to prevent

the formation of a hematoma and possible disruption of the wound. The drain should be removed in 24 to 48 hours. The subcutaneous tissues and skin are approximated in the usual manner.

In the meantime, the neurosurgeon will have exposed the cranial defect, and the bone graft now can be shaped and fitted to fill the skull defect. It has been our practice to bevel the edges of the cranial defect with a sharp chisel, so as to provide a new raw-bone surface against which to place the conversely beveled bone graft. Usually, the bone graft has fitted so snugly into the cranial defect that retaining sutures were not needed. Occasionally it has been necessary to use wire sutures to hold the graft accurately in place. These are secured by drill holes made through both cranium and graft, taking care to bury the cut ends of the wire in the bone to prevent irritating the scalp.

RESULTS

In this series of cases, 12 patients with moderate to large-sized cranial defects were selected for repair of their bony defect with split-thickness or full-thickness iliac bone grafts. All but one of the cranial defects had resulted directly or indirectly from severe trauma to the head. There were a number of depressed skull fractures that were grossly contaminated through a compounding injury. Three patients were operated on shortly after suffering a compound depressed skull fracture involving the frontal sinuses. In two of these, the cranioplasty was undertaken in the face of sinus infection without adverse results.

In every case, a satisfactory structural and cosmetic result was obtained with the iliac bone graft. One patient, who was operated on before the residual of a severe brain-stem injury had resolved, represents the one case of postoperative morbidity in our series. After operation, he had a pseudobulbar palsy that lasted for nearly four weeks before complete recovery ensued.

Pain from the donor site was usually more marked than pain from the site of cranioplasty. In one case, persistent iliac pain was coincident with a persistent fluid hematoma at the graft site. This disappeared entirely after 10 days, however, and in all the other cases iliac pain and pain from the cranioplasty site had disappeared by the third postoperative day. One patient, who had been immobilized for a long period because of an associated compound tibia fracture, developed thrombophlebitis after the postoperative period had elapsed. This was treated successfully with anticoagulants and mobilization.

CASE REPORTS

Case 1. A 6-year-old boy was hit on the side of his head with a pump handle, causing a large, compound, depressed skull fracture. This was

elevated on the day of injury, 13 May 1955, with removal of the bulk of the contaminated fragments. Neurologic recovery was complete, and the only remaining stigma was a large parietotemporal defect. On 5 August a right iliac bone graft was applied to the defect. The bony edges of the craniectomy site were prepared with an electric bur instead of the chisel and osteotome used in the other cases. The cosmetic result was satisfactory, and roentgenograms taken a year later indicated beginning calcification of the graft site.

Case 2. A 26-year-old staff sergeant received a head injury in a motorcycle accident on 2 July 1955. He had a compound, depressed skull fracture on the right. On 13 July he was transferred to this hospital, where the depressed skull fracture was elevated and a rather large extradural hematoma was evacuated. The patient, who was somnolent, disoriented, and lethargic, with a dilated right pupil, when he came in, recovered almost completely except for the cranial defect. Three months later, a split-thickness anterior iliac bone graft was applied to the craniectomy site. The immediate postoperative cosmetic result was satisfactory. Roentgenograms of the patient's skull taken postoperatively revealed a well-fitting cranioplasty, which did not necessitate retaining sutures. Because of legal complications, this patient had to be shipped back to the United States before an adequate follow-up examination could be made.

Case 3. A 20-year-old man was injured twice in a jujitsu wrestling match. He developed a right hemiparesis two weeks after his injury, and a craniectomy in the right parietal region was performed to evacuate a substantial subacute subdural hematoma. On 9 September 1955, a split-thickness iliac bone graft was used to repair the craniectomy defect. A one-year follow-up on this patient revealed a good cosmetic result. The patient had no complaints referable to his cranioplasty site, and had participated in swimming meets, without adverse effects. Skull roentgenograms done at this hospital revealed the obliterated defect in the right frontal parietal region with the bone graft in place.

Case 4. A 45-year-old woman fell down a flight of stairs, and suffered a compound, depressed skull fracture in the left frontotemporal region. During elevation of this fracture, a large extradural hematoma was visualized and evacuated. The patient, who preoperatively was lethargic and unable to carry out a rational conversation, recovered to a completely normal neurologic state. On 6 December 1955, the usual split-thickness iliac crest bone graft was used to repair the craniectomy site. This patient was seen 10 months later, before she returned to the United States. Her graft was solid and painless on palpation. The cosmetic result was satisfactory enough so that it permitted her to act as hostess for large, official military gatherings without apprehension as to her appearance.

Case 5. A 27-year-old man was injured in an automobile accident on 17 December 1955, and sustained a deeply depressed, compound, frontal

skull fracture. He had a large craniectomy in the frontal region with elevation of his depressed fracture and obliteration of the greater part of his frontal sinuses. On 6 April 1956, a right iliac split-thickness graft was used to repair the frontal defect. The patient had a further débridement of sinuses at the time of the cranioplasty. One sinus was packed with fat and the other with bone chips, for comparative test. The cosmetic result was considered to be excellent. In the postoperative period, the patient had severe attacks of maxillary sinusitis, but his frontal sinuses remained uninfected. The patient was asymptomatic on 26 December.

Case 6. A 3-year-old girl fell out of a second-story window and suffered a compound, depressed skull fracture in the right parietal region. The fracture was elevated and the inferior bony segments, which protruded into the brain, were removed. The patient had a plastic repair of her dura mater, after debridement of the cerebral wound. Although she was unconscious when she came in, with active bleeding from both ears, she recovered completely after this procedure and had no residual except for a craniectomy defect. On 27 June 1956, a split-thickness iliac bone graft was taken and a cranioplasty was accomplished. The result has been good. The patient remains asymptomatic, and a six-month recheck examination disclosed a solid graft without pain on palpation.

Case 7. A 23-year-old man had a granuloma of the skull with severe radiating headaches. A primary resection of this bony tumor and iliac graft were planned for 25 January 1956. A split-thickness iliac bone graft was taken from the left anterior crest of the ilium, but the patient suffered a cardiac arrest and had to be resuscitated by means of a cardiac pacemaker. On 3 February the cranial lesion was resected under local anesthesia and was found to involve the dura mater. The histologic diagnosis of granuloma, however, was made on rapid section, and total resection of the tumor was accomplished. The iliac bone previously taken and kept in the deep-freeze bone bank, was used for a cranioplasty. This patient, with a low pain threshhold, has had no complaints about either the donor site or cranioplasty, since the operation.

Case 8. A 20-year-old man was involved in an automobile accident in late May 1956, suffering severe head injuries. He was deeply unconscious, and began to have decerebrate seizures. The patient had massive brain swelling, and a bilateral temperoparietal craniectomy was performed on both sides, with a large free dural graft taken from the temporalis fascia to give a watertight dural closure. The patient gradually recovered consciousness over a period of several months, and his only residuals were a paralysis of upward gaze and signs of a frontal lobe disturbance.

On 24 July 1956, a full-thickness iliac graft was taken, and bilateral cranioplasty was carried out under general anesthesia. After this procedure, the patient suffered a pseudobulbar palsy with difficulty in swallowing, in jaw movements, and in tongue and facial movements,

along with some increase in the emotional lability that was present to some extent before the operation. His symptoms lasted for almost a month before gradually improving to the extent that he could speak English and German and could use with facility all the muscles enervated by the lower cranial nerves. This man, because of his severe central nervous system damage, was returned to the United States for prolonged hospitalization. At this time, both graft sites were well healed and solid to palpation.

Case 9. This patient was injured in an automobile accident in August 1936. He suffered a severe head injury with a depressed frontal skull fracture. He had no further difficulty except for his cosmetic disfigurement for 20 years (fig. 1A). On 16 August 1956, a right split-thickness iliac bone graft and cranioplasty were performed. The patient has done well and the graft has healed solidly (fig. 1B).

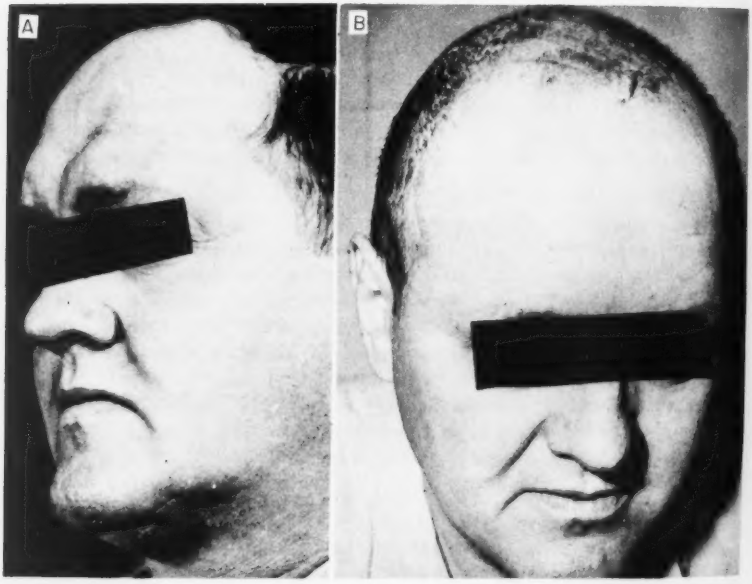

Figure 1 (case 9). (A) Cosmetic defect that resulted from an automobile accident in 1936. (B) Frontal view of the same patient, following iliac graft cranioplasty. Incisional scar follows the hairline.

Case 10. A 22-year-old man suffered a left-frontal, compound, depressed skull fracture on 27 July 1956, in France, when he was thrown out of a moving vehicle. The following day, an extensive compound depressed skull fracture in the left frontal region was elevated and loose, contaminated bone chips, which protruded into the brain, were removed. A resection of the involved cerebral tissue was carried out and the dural lacerations repaired. The patient had some personality

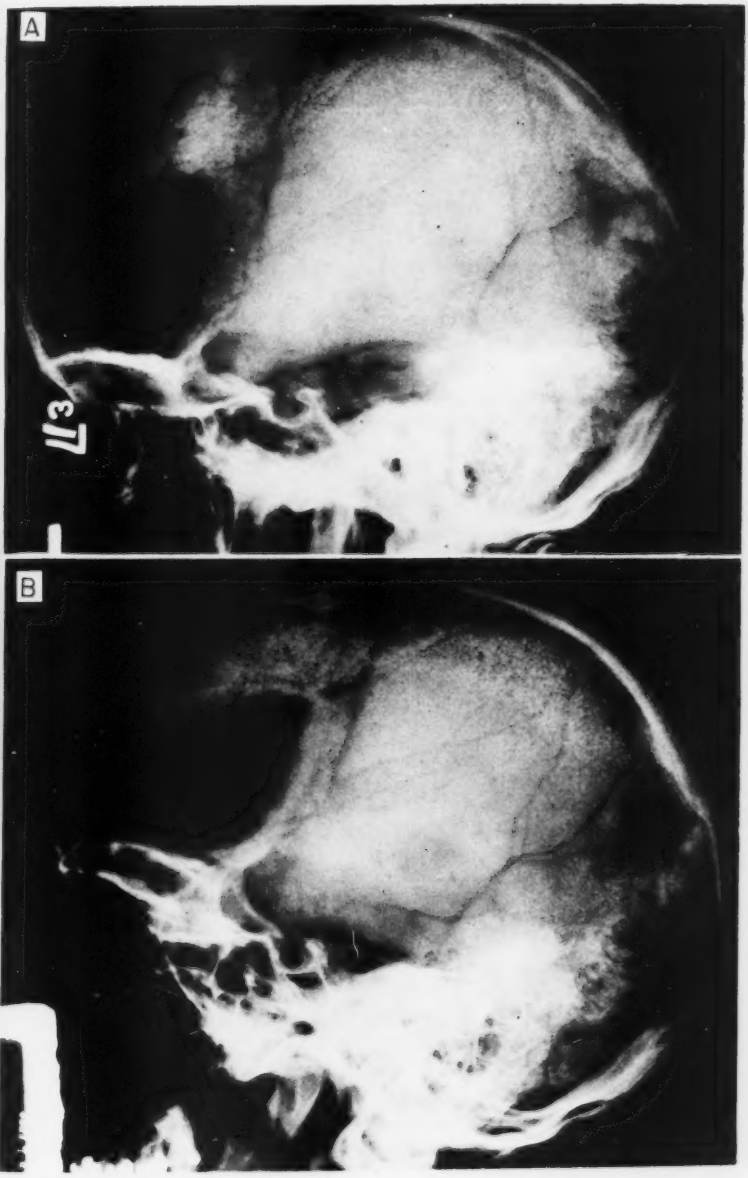

Figure 2 (case 10). (A) Roentgenogram showing cranial defect following the decompression of a compound skull fracture. (B) Roentgenogram taken two months after operation, showing bone graft uniting firmly with its recipient bed.

changes when he came to the hospital. These were difficult to evaluate because of alcoholism. His postoperative recovery was complete, except for a craniectomy defect (fig. 2A). On 21 September a right iliac bone graft was applied to the defect. The patient had an uneventful recovery from this procedure. On 27 November postoperative roentgenograms of the skull showed the graft wedged firmly into place (fig. 2B). Follow-up examination on 20 January 1957 revealed no change from the previous examination.

Case 11. A 24-year-old man was riding in an automobile that struck a tree. He suffered a large, compound, depressed skull fracture in the left frontal region. On 9 June 1956 part of his depressed skull fracture was elevated and contaminated fragments were removed. The frontal sinus on the left was obliterated. His postoperative course was uneventful, except for a recurrent attack of sinusitis. On 1 August radical frontal and ethmoid sinusectomy was carried out with complete relief of symptoms. On 17 October anterior iliac graft and cranioplasty were performed. (figs. 3A and 3B). The patient has been asymptomatic. On examination on 20 January 1957, his graft was firmly in place and he was well satisfied with the cosmetic result.

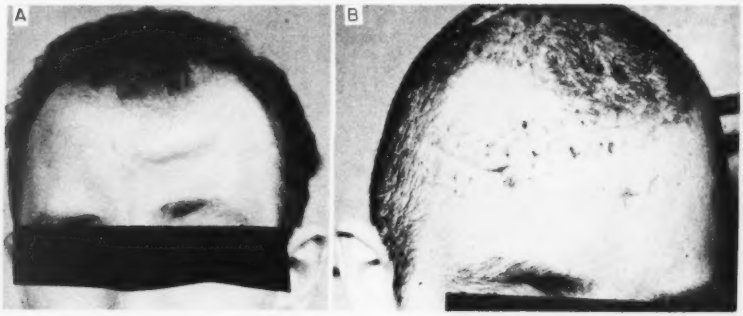

Figure 3 (case 11). (A) Cosmetic defect following a compound skull fracture of the left frontal bone. (B) Immediate postoperative view of the cosmetic result achieved by using iliac bone graft.

Case 12. A 21-year-old man suffered a compound, depressed fracture of the right and left frontal bones in an automobile accident. On 6 August 1956, some of the depressed fracture was elevated, but much of the contaminated segment had to be removed and both frontal sinuses were obliterated (fig. 4A). At the same time, a compound fracture of the medial shaft of the left tibia was débrided. On 24 October a full-thickness right iliac bone graft was applied to the craniectomy defect. The patient's postoperative course was complicated by thrombophlebitis and a single pulmonary embolus. He was kept on anticoagulants for three weeks, even though he was ambulatory. At the end of this time his thrombophlebitis had disappeared, and his postoperative course was without further incident. The right orbital ridge protruded too far

over the lateral portion of the eye, and on 14 December, under local anesthesia, the ridge was molded to give a better cosmetic result (fig. 4B). When the patient was examined on 11 January 1957, his graft was solid to palpation and the cosmetic result was satisfactory.

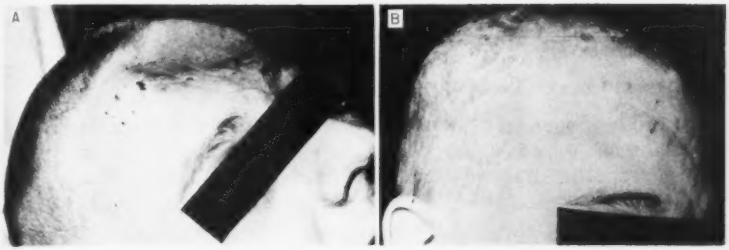

Figure 4 (case 12). (A) Marked depression of both frontal bones, following a compound depressed fracture in an automobile accident. (B) Contour restored by iliac bone graft cranioplasty.

DISCUSSION

A historical review of the repair of cranial defects is given in some detail by Grant and Norcross.[2] It seems obvious that the use of autogenous bone grafts to obliterate large cranial defects has been rewarded with a high percentage of successful results. Lambros,[3] in 1943, reported a case in which a large postoperative defect was repaired by a graft from the ilium, and discussed the literature on the subject. Even though this case was successful, Lambros believed that there were a number of disadvantages to the method. These included spontaneous fractures of the graft, alteration in gait caused by pain from the donor site, and a "Herculean surgical procedure" to obtain the graft and apply it to the cranial defect. He recommended methyl methacrylate as a substitute for autogenous bone grafts.

McClintock and Dingman[4] advanced a rather convincing argument in favor of autogenous bone grafts, and the points made in their article are ones with which we concur wholeheartedly, based on our own experience. We believe that the removal of the iliac bone graft is a rather minor procedure. In our experience, it proved to be traumatic in only one case, in which the patient suffered severe hypotension and cardiac arrest, which was quickly reversed with a cardiac pacemaker. This did not result in any neurologic or other deficit to the patient. This particular patient, however, was rather prone to hypotensive episodes. He fainted twice, before the operative procedure was carried out, and also had a very low blood pressure after lumbar puncture in preparation for doing a a pneumoencephalogram. He required an enormous amount of sedation subsequently, when a successful pneumoencephalogram was performed. The operative procedure in which the cardiac arrest occurred was carried out with a minimum of pain-relieving anesthetic agent, as the patient was given a continuous intravenous

drip of a curare-like agent. It is possible that he responded in an exaggerated manner to the surgical procedure because insufficient anesthesia was used.

In no case was there an excessive loss of blood during removal of the iliac bone graft. In only one patient was there any incapacity in the patient's gait, and this disappeared after the reabsorption of hematoma at the donor site.

Satisfactory cosmetic results following this type of cranioplasty were easy to achieve, because an abundance of bone could be removed from the ilium and the graft could be molded to the correct contour of the cranium. Furthermore, the graft could be shaped so accurately and the craniectomy site could be so well prepared that in many instances the bone graft could be fitted into the cranium and held in place without wires or other retaining materials.

There were no postoperative infections in any of our cases, even though most of the wounds had been badly contaminated at the time of the original injury, and the bone graft in four cases was inserted into the frontal sinus region. Two of these patients showed signs of frontal sinusitis at operation, yet the grafts have remained solid and there have been no complications to date. The chance of fracturing a well-healed bone graft seems remote. On the other hand, a recent report in the literature[5] indicates that large plastic or methyl methacrylate cranioplasty plates sometimes do fracture.

We wish to emphasize that this is an initial report on a series of patients who all have had satisfactory results. The longest follow-up to date is a year and a half. At the end of a five-year period, however, we intend to question and examine this series of patients, and write another communication on the observations to be made at that time.

SUMMARY

The initial repair of large cranial defects has been accomplished with the use of anterior iliac bone grafts. The initial impression, after operating on 12 patients, is that this form of bone graft provides a satisfactory structural and cosmetic result.

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CLINICAL EXPERIENCE WITH 682 CASES OF ASIAN INFLUENZA

LAWRENCE S. GREENE, *Lieutenant, MC, USNR*
THOMAS E. HAIR, Jr., *Lieutenant, MC, USNR*

INFLUENZA has affected mankind with varying intensity for many years, but only since the epidemic of 1933, when type A influenza virus was isolated, has this disease yielded to accurate laboratory as well as clinical diagnosis. In April 1957 influenza once again began one of its characteristic peregrinations,[1] spreading rapidly from Asia to Europe and the United States, and eventually involving most of the world.[2,3] The causative virus of this "Asian influenza" was identified as A/Japan/305/57.

The clinical material herein presented concerns 682 cases of Asian influenza seen during October and November 1957 in an epidemic characterized by sudden, dramatic onset in a select population of previously active, healthy, military personnel.

Symptoms. The frequency distribution of symptoms encountered in the 651 uncomplicated cases of influenza is charted in figure 1. Considered graphically, the symptoms appear to be non-specific, but distinct individual characteristics of the following six symptoms were easily discernible and contributed greatly to the facility with which the clinical diagnosis could be made:

Headache, characteristically dull, severe, and unremitting, located frontally or retro-orbitally, and often associated with marked somnolence, was a frequently repeated complaint.

Fatigue, overpowering in nature, causing healthy young men to become incapable of performing their duties, was prominent.

Cough, typically dry, irritating, and not productive of any type of sputum, was characteristic.

Chills, more correctly frank rigors, was a dependable, readily recognized symptom.

Ocular pain, aggravated by any and all motion of the eyes, and leading to minimal use of the eyes, was an unmistakable finding.

From U. S. Naval Hospital, Memphis, Tenn.

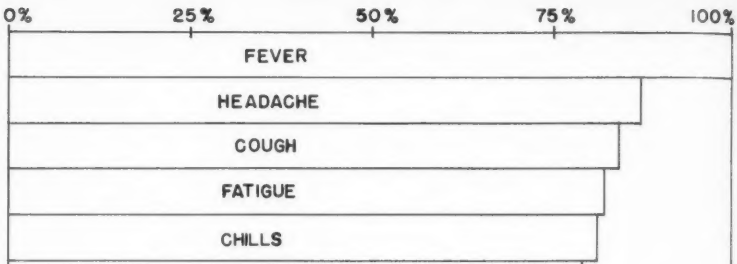

Figure 1. Frequency distribution of symptoms in 651 uncomplicated cases of Asian influenza.

Myalgia, referred to the low back area, was an often-repeated complaint of a large number of patients.

In contrast, other common symptoms such as soreness of the throat, chest pain, anorexia, nausea, and vomiting were notably insignificant.

Physical Examination. The findings on physical examination of the chest, including inspection, palpation, percussion, and auscultation, were strikingly negative, with a total lack of localizing signs. Very rarely were minor scattered rhonchi, occasional wheezes, and less frequent discrete rales heard. Plethoric facies associated with elevated temperatures were found uniformly. Pharyngeal injection, nonspecific in type, and associated with discrete, mobile, slightly tender cervical lymph nodes, was common.

Laboratory Studies. Laboratory findings were nonspecific and of little diagnostic value. Because of the dramatic acuteness of the epidemic with involvement of a large number of our labo-

ratory personnel, bacteriologic studies were of necessity minimal. Hematologic observations revealed normal hemoglobin. The white blood cell count generally was found to be between 5,000 and 9,000 per μl, with little in the differential count that varied from normal. No shift to the left was noted; however, a relative lymphocytosis was observed frequently. Urinary abnormalities were infrequent; albuminuria occurred in 3 cases, microscopic hematuria in 8, and microscopic pyuria in 14. Subsequent studies revealed that these abnormalities cleared spontaneously. Roentgenograms of the chest were taken on all patients. Chest films measuring 14 by 17 inches were obtained in 519 cases; the remaining 163 had 70-mm chest films. In uncomplicated cases of influenza the chest films were uniformly normal.

Shortly after the onset of the epidemic, blood specimens were drawn from 16 patients, including the first 10 seen, in order to determine the nature of the afflicting virus. Subsequently, when the clinical pattern of the epidemic had become obvious, only 1 patient from each 100 was studied serologically. A fourfold or greater increase in antibody titer in the convalescent specimen as compared to the acute-stage specimen was considered positive evidence of infection by the agent whose antigen was used in the test. The results of these studies, performed by U. S. Naval Medical Research Unit No. 4, Great Lakes, Ill., indicated that the offending agent was the Asian influenza virus, A/Japan/305/57.

Effect of Vaccination. Vaccination of local military personnel was begun as soon as the polyvalent vaccine with Asian strain included became available for wide-scale use in the area. Personnel were immunized on one occasion by intradermal injection of 0.1 ml in each arm. Of the 682 patients with influenza in this series, 376 (55 per cent) had not been immunized, 201 (30 per cent) had been immunized one week before they became ill, and 105 (15 per cent) had been immunized two weeks prior to the onset of illness. There was no discernible difference in clinical picture, complications, or course of the disease between the immunized and nonimmunized groups.

Temperature Curve. As shown in figure 2, 91 per cent of our uncomplicated cases had a temperature curve characterized by a progressive downward trend, reaching normal levels in 48 to 72 hours without salicylate therapy. This failed to occur in 9 per cent of the cases, being replaced by a persistent febrile response which waxed and waned, finally reaching normal after five to seven days of hospitalization.

Nature and Frequency of Complications. As is well recognized, the principal dangers in an influenza epidemic lie in the complicating illnesses. Those that developed in this series are enumerated in table 1.

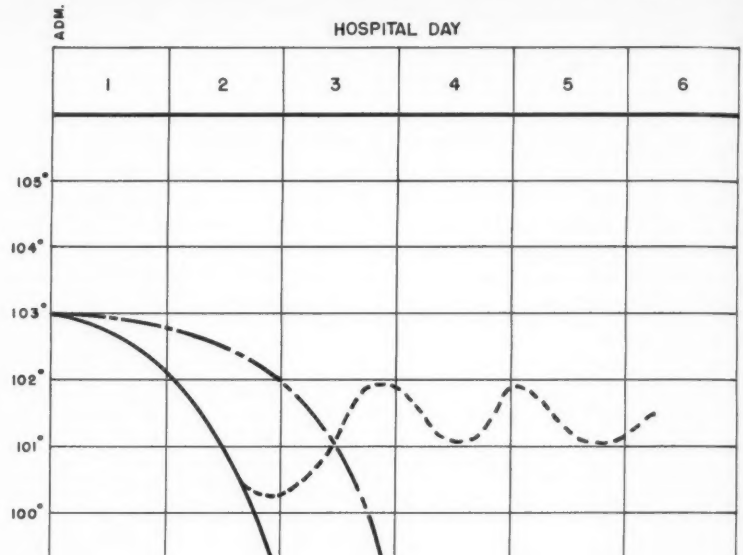

Figure 2. Variations in temperature response in 651 uncomplicated cases of Asian influenza.

TABLE 1. *Complications seen in 682 cases of Asian influenza*

Complicating illness	Number of cases	Incidence (per cent)
Bronchopneumonia	17	2.5
Otitis media	7	1.0
Bronchitis	4	0.6
Sinusitis	3	0.4

We considered the term "complication" to imply the development of an illness of the type listed in table 1 after infection with the influenza virus as characterized by the previously described clinical symptoms. The most important clinical aid in

detecting a developing complication was the characteristic temperature response which occurred, provided that continuous salicylate therapy was not employed. Every one of the 31 patients in our series who developed a complicating illness failed to become afebrile in 72 hours. Their temperature curves waxed and waned, returning toward normal only after six to seven days.

Although this type of response was exactly like that found in 9 per cent of the uncomplicated cases in this series, as shown in figure 2, it provides an urgent clinical warning to the practicing physician. When such a febrile response is encountered, careful re-evaluation of the case with appropriate diagnostic procedures, including the necessary radiologic technics, is in order, to rule out the presence of a complicating infection.

Therapy and Length of Hospitalization. The principal treatment of uncomplicated cases in this series was bed rest, supported by fluids of all types administered by mouth in large quantities. Simple expectorants were used, and where indicated, mild analgesics and nasal decongestants were employed. Parenteral fluids and alcohol sponging were utilized only for severe febrile responses. With this simple but effective regimen, the average hospital stay was six days. Indeed, in uncomplicated cases, it was obvious that hospitalization was necessary only as an epidemiologic control measure.

There has been much recent emphasis on the failure of antibiotics to prevent the pulmonary and other complications of viral diseases,[4,5] including poliomyelitis, measles, the common cold, and influenza. Moreover, the harm that may arise from widespread use of antibiotics in influenza has been stressed on numerous occasions.[6,7] It has been shown that despite the total ineffectiveness of antibiotics against the influenza virus, they frequently are effective in combating the potentially fatal bacterial complications of the respiratory tract which may result from this disease. However, with the routine use of antibiotics prophylactically in such an epidemic, the result may be the widespread development of antibiotic-resistant infections. Accordingly, we used only symptomatic therapy in all cases of this series, with the exception of appropriate chemotherapy when a distinct complication attributed to secondary infection occurred.

This clinical study convinced us that complications arising from influenza are easily and accurately recognized by clinical means. Provided sustained antipyretic therapy in the form of salicylates is not employed, a characteristic febrile response provides a reliable clue to the presence of a complication. When such a febrile reaction is observed, the physician must carefully reappraise the situation and begin a diligent search for the locus

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of a secondary infection. Once discovered, the complication can be effectively treated.

Of secondary importance, inexpensive, readily-available medications are adequate for successful therapy of influenza, without necessitating undue financial strain on the patient.

SUMMARY

A clinical study was made of 682 cases of influenza seen in a sudden epidemic in a military population and serologically confirmed as caused by the Asian influenza virus. It was found that the disease presented a distinct symptom complex which made possible accurate diagnosis on a clinical basis. Physical and laboratory findings tended to be insignificant in uncomplicated cases. In 91 per cent, the temperature decreased steadily to reach normal in 48 to 72 hours, but in 9 per cent it fluctuated between 101° and 102°F for several days. Immunization either one or two weeks prior to onset of the illness had no discernible effect on the clinical picture or course of the disease.

Symptomatic treatment without use of antibiotics resulted in rapid recovery with no fatalities. Complications in 4.6 per cent of the cases were successfully treated with antimicrobial agents. In every case in which salicylates were not being used extensively, the presence of a complication was heralded by a characteristic fluctuating temperature curve, providing a clear warning that search should be made for a possible complication.

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GROUP THERAPY WITH MEDICAL PATIENTS

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EUNICE L. CUNINGHAM

AT a large military base, a shortage of psychiatrists results in a situation where therapy is necessarily minimal. Such a problem exists at this hospital. One psychiatrist and one psychiatric social worker comprise the neuropsychiatric staff. With from 35 to 50 admissions to the Psychiatric Service per month, and an average of about 200 consultations each month, the psychiatrist can do little more than categorize and transfer to larger psychiatric units most of the patients in need of therapy.

PROBLEM

Keenly aware of the need for a psychiatric approach to certain medical problems, several members of the Department of Medicine, together with the psychiatrist and the medical social worker, decided to formulate a more complete therapeutic program for so-called psychosomatic cases. It was apparent that the psychiatrist had little time to participate in the treatment of patients on other services. It also was clear that personnel with little training in psychiatric procedures, especially those related to therapy, would flounder somewhat aimlessly in any psychotherapeutic endeavor undertaken without the guidance of a psychiatrist.

METHOD OF INDOCTRINATION

Twice a week for six weeks, the psychiatrist met with two members of the Department of Medicine and the social worker assigned to their wards for 1½ to 2 hours of indoctrination. The aim of these sessions was to establish certain guides in group therapy. Because only a few ideas could be well established in the limited time, the psychiatrist devoted these sessions exclusively to a study of the emotions, and in a general way elucidated their manifestations in those suffering from psychosomatic illnesses. Principally stressed in the psychodynamic genesis of these disorders was the modus operandi of hostility. An attempt was made to promote insight into the process by which hostility, deviously expressed, is transposed into physical complaints and symptomology. The detection of concealed

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hostility was emphasized by study of verbalizations and by observation of attitudes and physiologic responses—postural, facial, vascular, et cetera.

To orient those conducting the group sessions and to establish goals in the minds of the patients, introductory approaches to group therapy were reviewed and attention was invited to the necessity of promoting an emotional rather than an intellectual atmosphere. The role of the therapist was presented as that of a catalyst, accelerating the production of emotional material; the expressions of the feelings of disturbed patients. The formulation of meanings in terms of illness and health was to be derived from this material. Principally avoided were the academic formulas of the classical psychiatrists. Jargon, such as ego, id, castration complex, Oedipus situation, anal, oral, and similar terminology was rejected assiduously. Family situations were examined, especially those in childhood that may have been conducive to the generating of fear with its attending hostility reactions. Attitudes towards one's self and towards others were presented as reflections of feelings promoted in the relationships of the patient to those in authority. These attitudes, and their attending affective reactions, were illustrated, and the chronology of specific cases was used to facilitate emotional understanding.

SELECTION OF PATIENTS

Between December 1955 and February 1957, seven psychotherapeutic groups were organized on the Medical Serv . One group consisted of nine mothers of children with enure. that was suspected to be of a psychogenic nature. The remaining six groups were made up of a total of 63 patients from two medical wards, with various medical illnesses that were considered to be psychosomatic in nature. The diagnoses included peptic ulcer, tension headache, psychogenic cardiovascular disease, neurodermatitis, ulcerative colitis, rheumatoid arthritis, and bronchial asthma. Thirteen of the 63 patients were diagnosed as having peptic ulcer.

The two medical officers selected the patients after completion of medical studies. Only those patients with apparent psychopathology were selected, and an attempt was made to eliminate those not considered well motivated to profit by the experience. Ages ranged from 17 to 55 and the average was 28 years. Length of service varied from 6 months to 26 years, averaging 6 years. Rate included seaman to chief. Eight of the 63 patients were chiefs and 3 were first-class petty officers. A minimal social evaluation of each patient was made by the social worker and presented to the medical officer concerned, preliminary to the acceptance of the patient into group therapy.

Each group of medical patients had an average of ten patients. The groups met an average of 11 times in 2-hour sessions, twice a week. The leaders were one of the two medical officers and the medical social worker. The group sessions were held in a private office removed from the medical ward. An effort was made to promote an informal and casual atmosphere. In some of the groups new members were added as old members were discharged to duty.

PROCEDURE AND RESULTS

Ground rules, which were established with the idea of making each patient as comfortable as possible, were as follows: (1) rank was not to exist within the group; (2) all material presented was to be considered confidential within the group; (3) each patient was to be privileged to talk or not talk as he pleased, or to come and go as he wished during the sessions; (4) each patient was to be encouraged to express himself as he wished. Throughout the period of the study, the two ward medical officers and the social worker met with the psychiatrist once or twice a week to discuss the emotional situations engendered within each group.

In general, the process which evolved in each of these groups followed a similar pattern. Each patient was informed that he had been especially selected for this extra prescription, but was privileged to refuse it or to discontinue it at any time. All 63 patients accepted immediately, and only 5 discontinued before completion.

During the first meeting, the medical officers were asked many questions, and they freely gave medical information in terms that the patients could understand. The doctors and the social worker gave a preliminary explanation of ways in which feelings cause inner tension, and the physiological effects were outlined. An effort was made in the initial meeting to convey some meaning to behavioral and emotional patterns. The value of examining our feelings and actions for the express purpose of understanding ourselves, was emphasized. This understanding was represented as a means of accepting ourselves, thereby experiencing less tension, less anxiety, and, therefore, less illness.

After the patients had satisfied their curiosity about their particular illness and had gained new knowledge of ways in which they were promoting their illness, they appeared eager to talk about themselves. Items discussed included the patient's interpretation of his illness, his feelings about the treatment, and his explanation of the causes. Attention usually moved to the patient's early life, to the significant figures in his development, and to his feelings toward these persons. After approximately four meetings, the patients generally were com-

municating freely with each other, agreeing and disagreeing, beginning to see in others emotional causes for their illnesses, as well as some of their resistances to giving up old habits and emotional patterns. After about five sessions, many of the patients began to experience a gleam of insight into their difficulties and to express their acceptance of this insight to the group.

Gradually, the group processes and group feelings changed, so that the staff leaders were participating to a minimum. Natural leadership within the group began to take over the direction, the patients showing less concern over what the staff leaders and other members thought of them as they began to operate more openly in their verbal and nonverbal communication. Friendships were established and the group-communications continued in smaller groups on the wards. Feelings of responsibility to each other began to emerge, and self-understanding from an emotional viewpoint commenced to gain stature as a goal, in the approach to emotional and physical health.

During this group-process, patients were observed to become comfortable enough within the structure of the group to express their fears of making mistakes, their feelings of being mistreated whenever reprimanded, their exaggerated suspiciousness, and their feelings of failure, worthlessness, and lack of self-esteem. These expressions promoted awareness of kindred patterns of emotional reaction in the lives of each of us. Slowly but definitely a sense of humor began to permeate; and, above all, a degree of self-acceptance.

It is interesting to note that the basic philosophy of social work was brought into operation within the groups. This philosophy includes belief in the basic worth and dignity of each person, the right of self-determination, the importance of nonjudgmental attitudes, and the ability for change and growth inherent within everyone.[1] The tone of meeting after meeting expressed this basic thinking and was reflected in remarks heard first from the group leaders and quickly picked up and used constantly by the patients about themselves and others—such remarks as "It's OK to be human, you know." "Why can't you forgive yourself?" "Why do you have to be always perfect?" "It's all right to be all wrong at times."

Hostility and resistance were more apparent in the early meetings, and were encountered usually in the form of skepticism, disbelief, doubt, silence, et cetera. Such statements as "This stuff is a lot of bunk." "What has my childhood got to do with my headaches?" "How are you gonna talk me out of my stomachache?" are examples of these reactions.

Some patients experienced immediate and dramatic relief from anxiety during the group process. For example, a Negro

who had suffered with asthma nightly for four months, and who came to his first meeting in a wheelchair, breathing heavily, became completely asthma-free while ventilating extreme hostility towards recent authority. He was given support by the medical officer as well as by the group members. He remained asthma-free for the following four weeks in the hospital. Another patient with tension headache was amazed by his feelings of relief, after ventilating the hostility he had experienced in childhood towards his step-father, concomitantly with his expressions of hatred towards his commanding officer.

It is interesting to note that the majority of these 63 patients expressed positive feelings toward mother, and negative towards father. In fact, more than 40 of the group openly expressed resentment, anger, and fear in re-experiencing their feelings of being unfairly and oftentimes abusively treated by their male parent. Many patients were able to help others relate their present reaction to authority to the early emotional patterns of childhood. As an illustration, one patient was admitted to the hospital with hypertension of a degree that made it impossible for him to re-enlist. He was able in group therapy to associate a recent reaction to a reprimand from his commanding officer to his extreme fear and hatred of his father as a child. The commanding officer had called the serviceman to his office a few days prior to his re-enlistment time and had talked to him about an outstanding bill, long overdue. The serviceman had planned to use his re-enlistment money to pay off the bill and other accumulated obligations. In group sessions, this young man was supported by other members and encouraged to talk about himself. He poured out long-repressed feelings of resentment toward his father who had left his mother while the serviceman was a child, with resulting financial deprivation to himself and his siblings. With some direction from the group, he began to understand the relationship between his earlier emotional reaction to his step-father and the present disproportionate reaction to his commanding officer's reprimand. His blood pressure began to improve and eventually he was able to pass his physical examination for re-enlistment.

Another patient, a 17-year-old seaman, was admitted to the hospital with tension headaches. He had been in the service for seven months. He told of being the oldest child in a large family. His father was described as erratic and the patient expressed feelings of great concern over the welfare of his mother and younger siblings. He dreamed of his mother almost nightly. As he talked, members of the group began to see the connection between his anxiety about getting out of the service to help his family and the feelings of inadequacy he had experienced in his earlier home environment. He told of repeated

incidents, in the service, of his feelings of being picked on because he was the smallest man in his outfit as well as the lowest in rate. In subsequent group meetings he was placed affectionately in the role of the kid brother of the group. He began to feel a sense of union with the other members and to experience a feeling of security in this situation. He began to appreciate the value to his own personal growth and development of remaining in the service, of learning to adjust to life away from his mother, and of experiencing satisfying relationships and accomplishments which are possible in the Navy. He finally expressed the fact that it was quite possible that he could help his mother more financially by remaining in the service than by going home. He discontinued to dream of his mother and his headaches went away. He asked his doctor, the co-leader of the group, to return him to duty and to help him get back to his former duty station.

Of the 63 patients, only 5 discontinued attending the group prior to its completion or their discharge from the hospital. A total of 54 patients reached a mutual decision as to their return to active duty and one of the requisites for return to duty was improvement in symptomology to warrant a designation, "fit for duty." The number of patients discharged from military service during this period of group therapy was markedly diminished on the two medical wards involved. Treatment of these medical patients by means of group communication was the only change that had occurred during this period.

The seventh group conducted during this period concerned a group of 9 mothers with children suffering from enuresis for which no organic basis could be found. Each child was given neurologic and electroencephalographic examinations by the psychiatrist. Following the medical work-up, the mother was referred to the social worker for an individual social study before she was added to the group. In addition to the 9 children with enuresis, these 9 families included 20 other children, some of whom suffered from stuttering, eating difficulties, sleeping irregularities, and behavior disturbances. The mothers ranged in age from 21 to 35. The group sessions were conducted by the two medical officers and the medical social worker who had worked with the medical groups. Again they acted as co-leaders.

A form was given to each mother in the last session, or tenth meeting, in an effort to measure the results. Information on these forms, which were mailed back to the social worker, indicated that every one of the enuretic children had shown improvement, several becoming dry at night for the first time. Plans have been made to have follow-up meetings with this group of mothers to ascertain if the initial improvement is sustained. A check on the outpatient charts shows a decided decrease in clinic visits, following this period of group therapy for these families.

SUMMARY AND CONCLUSIONS

A program has been outlined whereby a psychiatrist has utilized nonpsychiatric personnel in a group therapy program involving medical patients. During the therapy these patients at no time were under the direct observation of the psychiatrist. The two medical officers and the social worker leading the group sessions were given a specific type of indoctrination by the psychiatrist, who then met with them biweekly to evaluate the emotional material produced in the group relationships. The following conclusions were reached as a result of this study:

1. The function of a psychiatrist in a general hospital can be greatly enhanced by assimilating nonpsychiatric personnel into a therapeutic program that involves other than patients under his direct supervision.

2. It is possible by brief but adequate indoctrination for medical and associated workers to conduct effective group therapy with psychosomatic patients.

3. Group therapy by nonpsychiatric personnel must be continuously under the guidance of a psychiatrist.

4. Medical men, regardless of specialty, may utilize to the advantage of their patients the technics of group therapy in a controlled situation.

5. The group communication method is an effective one for bringing together quickly, easily, and naturally the medical, psychologic, and social factors of individual cases.

6. The morale of a medical ward improves when group therapy is utilized.

7. Patients who participate in group therapy probably experience a more lasting recovery than would be possible by the use of medications alone.

ACKNOWLEDGMENT: The authors are grateful to Lt. Comdr. Woodrow Batten, MC, USNR, and Lt. Comdr. Leo Nastasi, MC, USNR, for their active participation in this study.

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NEW ASSISTANT FOR DENTAL SERVICES, USAF

Brigadier General James S. Cathroe, USAF (DC), has been appointed Assistant for Dental Services to succeed Major General Marvin E. Kennebeck, USAF (DC), who retired on 31 January 1958, after more than 33 years of service, it was announced by Major General Dan C. Ogle, USAF Surgeon General.

A native of Omaha, Nebr., General Cathroe received his Doctor of Dental Surgery degree from Creighton University Dental School in 1928. He entered on active duty with the Army that year and served his internship at Letterman General Hospital, San Francisco, Calif.

General Cathroe transferred to the Air Force in July 1949 where his assignments have included duty as Command Dental Surgeon of Eastern Flying Training Command, Caribbean Air Command, and Air Training Command. He was appointed Deputy Assistant for Dental Services in 1955.

General Cathroe

General Cathroe is a member of the American Dental Association and the *Federation Dentaire Internationale.*

World Health Day

The traditional date of World Health Day, 7 April, will mark the tenth anniversary of the World Health Organization. This day should serve to review and publicize the strides made toward the WHO goal—"the highest possible level of health," which has been achieved during the past decade of national and international effort made possible through the co-operation of local, national, regional, and international health organizations.

These achievements—in the form of new technical means, intensified educational programs, improved health legislation, and expanded facilities for the rapid exchange of medical information—are the substance of a collection of articles published by the WHO heralding "Ten Years of Health Progress."

Future issues of the *U. S. Armed Forces Medical Journal* will reproduce important parts of these articles that are considered of paramount interest to our readers.

Clinicopathologic Conference

U. S. Air Force Hospital, Wright-Patterson Air Force Base, Ohio*

FATIGUE

Summary of Clinical History. Approximately 1 to 2 years before admission, the patient, a 73-year-old woman, noted the onset of increasing exertional dyspnea, fatigability, brownish pigmentation and dryness of the skin, epilation, progressive bilateral deafness, stiffness of the neck and elbows, and intermittent anorexia. She was first seen by a physician about 9 months before admission, complaining of hearing loss, pruritus ani, and fatigue with vague complaints of nocturia and edema during the previous year. She recalled having been told that her blood pressure was elevated 25 years before this visit. Physical examination now showed a pressure of 200/110 mm Hg. She was treated with rauwolfia. Within one month she noted vitiligo and progressive edema, particularly involving the face, periorbital tissue, and head. This was diagnosed as hives and treated with antihistamines. The patient's blood pressure was then 170/90 mm Hg. A few weeks later she consulted her physician because of marked cyanosis, pain, and ulceration in her finger tips. She was treated with Priscoline (brand of tolazoline hydrochloride) and in two months the fingers healed.

Four months before admission she was observed to have 3 plus edema of the legs with a blood pressure of 140/70 mm Hg. She complained of generalized aching and stiffness, diagnosed as "flu," for which she was given an injection. The aching and stiffness persisted, however. Urinalysis showed a trace of albumin and a few white blood cells. Sedimentation rate was 40 mm

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*Col. Edward L. Olson, USAF (MC), Commander. From the Medical Service, Maj. John B. Logan, USAF (MC), Chief.

per hour and the hemoglobin was reported as "80 per cent." Salicylates and Gantrisin (brand of sulfisoxazole) had no effect and the patient became progressively weaker, so cortisone was started. The dosage was reduced after 10 days (from 100 mg to 50 mg) and her symptoms returned. After two weeks the patient became dizzy and cortisone was discontinued. Meanwhile her skin was noticeably dry and a deepening pigmentation developed over her arms.

Six weeks before admission her sedimentation rate was 18 mm per hour and urine was reported as normal. Within a week she developed, in addition to her other symptoms, headache and a return of her blood pressure to 215/110 mm Hg. Urinalysis showed 3 to 4 plus albumin. A second urine showed 3 to 4 plus albumin with many red and white blood cells. Her weight had not changed recently and was 135 pounds.

Physical Examination. The patient was a well-developed, well-nourished, 73-year-old woman, who was weak but alert. Her temperature was 98.6° F; pulse, 100 and regular; and blood pressure, 194/98 mm Hg. There was pitting edema of her forehead, sternum, spine, and legs, with marked puffy edema of periorbital tissue. Stiffness of the left sternomastoid muscle, and flexion contractures of both elbows were present. Minimal retinal arteriovenous nicking was noted. Reflexes and sensorium were normal. The skin was dry with pronounced dark-brown pigmentation and vitiligo of the index fingers.

Laboratory Studies. The urine had a specific gravity of 1.010, 3 to 4 plus albumin, variable numbers of red and white blood cells, and hyaline and granular casts. The Fishberg concentration test yielded specific gravities of 1.010, 1.010, and 1.012. Hemoglobin was 10.5 grams per 100 ml; hematocrit, 31 ml per 100 ml; and white blood cell count, 12,400 with 73 per cent neutrophils, 22 per cent lymphocytes, 2 per cent monocytes, and 3 per cent eosinophils. Total serum protein was 5.1 grams per 100 ml with 2.1 grams albumin and 3 grams globulin. Serum calcium was 8.0; inorganic phosphorus, 5.4; and urea nitrogen, 45 mg per 100 ml. Serum electrolytes were normal.

Roentgenograms of the chest disclosed pulmonary fibrosis, emphysema, and moderate cardiac enlargement; those of the fingers, elbows, et cetera, slight osteoporosis. Electrocardiograms showed sinus tachycardia and nonspecific abnormalities.

Course in Hospital. The patient ran an intermittent low-grade fever, not over 100°F. She was given a low salt diet, vitamins, Priscoline, and analgesics, and did well until the fourth day when, after eating, she complained of aching in the maxillary sinus area, gas and discomfort in the stomach, and shortness of breath. She also had a nonproductive cough. Blood pressure was

210/110 mm Hg. Apparently the symptoms cleared up quickly. The following evening the abdominal distention returned, but this time with severe periumbilical and suprapubic nonradiating pain, breathlessness, and cold sweating. The attack was relieved in 45 to 50 minutes with codeine and Nembutal Sodium (brand of pentobarbital sodium). Blood pressure was 190/110 mm Hg, and pulse 140. There were two more such episodes during the night. The patient continued to have weakness, tachycardia, shallow tachypnea, and occasionally flatus and vomiting. She was given cortisone, oxygen, parenteral fluids, digitalis, Thiomerin Sodium (brand of mercaptomerin sodium), and Terramycin Hydrochloride (brand of oxytetracycline hydrochloride). On this therapy the edema decreased but she developed hemoptysis, and rales and diminished breath sounds at the left base. Her condition continued a downhill course. Corticotropin was substituted for cortisone. Twenty-four hours before her death, the patient developed a watery diarrhea which was thought to be caused by Terramycin. She died on her 11th hospital day.

DISCUSSION

Doctor Sillman:* There are two people to discuss today's protocol; the first is Doctor Joseph Claro.

Doctor Claro:** A notable feature of this case was the disquieting regularity with which I found myself jumping at conclusions. In looking over the 15 to 18 symptoms, I tried to group the ones which I thought fitted a picture, and from that picture attempted to derive some sort of diagnosis. The symptoms I thought of significance were exertional dyspnea, edema that became progressive, easy fatigability, and a probable 25-year history of hypertension.

On admission the patient's blood pressure was 200/100. Pain and ulceration of her finger tips, from which she recovered with the use of Priscoline, certainly reflects a vascular problem. She had a history of albuminuria. There was a fair variety of other symptoms, which I think contributed to, rather than made, the diagnosis. One was, of course, her dry skin. This was probably due to senility. At first I thought the pigmentation quite significant; in fact, I compiled a rather impressive list of possible diagnoses based on pigmentation, but after researching to some extent I found that it often indicated, in an elderly individual, a sign of coronary disease. The fatigability and epilation went along with senility. The type of epilation was not mentioned, so I presumed that it was a generalized or splotchy loss of hair.

I do not think that either the progressive deafness or the stiffness of the elbows enter into the picture of her fundamental disease.

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**Capt. Joseph Claro, USAF (MC), Resident in Aviation Medicine.

Roentgenograms revealed some osteoporosis, which is probably related to her age, as is the arthritis and the pruritus ani. Intermittent anorexia is often due to gastritis, which in turn is present in certain kidney diseases, one of which I believe this patient had.

The physical examination states that the patient was well nourished, but there was no comment on the severity, frequency, or duration of her intermittent anorexia. It did comment that she had lost no weight recently. I assume that the statement, "well nourished" would be in keeping with her age. Except for one reading of 140/70, the blood pressure was consistently elevated, both by history and on physical examination. The pitting edema was certainly significant, suggesting some recent cardiac failure. The only comment on the retinal examination was that she had minimal arteriovenous nicking. A 73-year-old woman with a "25-year history of hypertension" and only arteriovenous nicking probably had intermittent hypertension. I assume she had normal neurological findings.

There were gaps in the history; one was that on the initial examination there was no comment on the physical findings in her chest. With what appears to be a moderate amount of congestive failure, there should be some findings. There were no comments on the heart sounds. A roentgenogram revealed moderate cardiac enlargement. I would expect some murmurs, if only functional ones. There were no comments on the condition of the vascular system. The fact that she had ulcerations on the tips of her fingers some months before and that they had healed with Priscoline treatment suggests some kind of vascular spastic disease. There was no comment on whether she had pipestem arteries, the condition of the brachials or radial pulsation.

The laboratory features reveal a little more of the situation with which we are dealing. The low specific gravity of the urine (two readings of 1.010 and a reading of 1.012) suggests marked loss of ability to concentrate the urine. This would be consistent with some sort of nephritis. Microscopic hematuria and white blood cells were noted in the urine, as well as albumin and casts. The hemoglobin of 10.5 grams represents a slight anemia consistent with the general illness found in these nephritic conditions. Her blood urea nitrogen was elevated to 45 mg per 100 ml. Doctor Sillman stated that a previous reading was lower than this, indicating progressive accumulation of nitrogenous waste products. The depressed serum calcium and the elevated phosphorus are consistent with nephritis.

In elderly patients, persistent sinus tachycardia as shown in the electrocardiogram may be evidence of coronary disease of long standing. The total protein was low with inversion of her albumin-globulin ratio. This doesn't seem to fit the diagnosis which I had in mind; however, I don't think its being there will necessarily rule out the conclusion. During her hospital course, she developed a mild fever which might well be attributed to a developing pneumonia. I recall no other indication of an infectious process. The protocol mentions severe ab-

dominal pains. In reviewing the literature I found something that I have never seen, but have heard about; that is, angina abdominis. This is a condition of abdominal pain, apparently very similar physiologically to angina pectoris. Angina abdominis is generally relieved with mild narcotics and sedation. These drugs relieved the patient, which supports this hypothesis.

In summary, this patient had hypertension on admission, and probably had had it for a long time. She had nephritis and probably coronary insufficiency. Hypertensive cardiovascular disease is common in people of this age. The one diagnosis that seems to tie all these things together is an arteriolonephrosclerosis. The finding against it is that the patient had edema, and the disease is a chronic nonedematous form of Bright's disease. The patient may have had a chronic nonedematous form, with edema due almost solely to cardiac failure rather than the nephrosclerosis. This is the diagnosis I offer—arteriolonephrosclerosis, with the other changes due to senility. Possibly she died of the uremia; maybe she had a pneumonia.

Doctor Sillman: Thank, you Doctor Claro. In looking over the chart, there were two blood urea nitrogen tests recorded. The first, on about her third hospital day, was 25, and the second (and last), on about the eighth day, was up to 45 mg per 100 ml. She died about five days after that. Her urine output was rather small, averaging 200 to 400 ml. Before we go any further, could we see the roentgenograms, Doctor Watts?

Doctor Watts:* Most of the time, the sicker the patient, the poorer the films. It is true in this case. The first two films were made, I assume, before the patient became ill. They reveal an enlarged heart, the configuration indicative of left ventricular enlargement. There is no pulmonary congestion at this time. Could I find out when she became ill?

Doctor Sillman: About one and one-half to two years ago. The symptoms before that were quite vague—present perhaps for another year.

Doctor Watts: Now we come to portable studies which were made when she was acutely ill—notice the heart has increased in size. Much of the apparent heart enlargement may be due to the fact that these are portable films. There is no date on any of the portable studies. Now, notice her lung picture. She had definite pulmonary congestion. The pulmonary vessels are fuzzy, indicating pulmonary edema, especially marked in the right base. The interlobar fissure is thickened. The next film shows essentially the same findings. In our last film the edema is more pronounced (fig. 1). She had edema of the left lung also, plus pulmonary congestion. We have a single film of the abdomen which technically is very poor. I see no pathologic condition except the asymmetry of the pelvis, which may have been due to an old injury. There are some mottled areas of increased density in both upper

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quadrants which I assume are artifacts. I think the roentgenograms indicate hypertensive cardiovascular disease with congestive failure, pulmonary edema, and in one film, radiolucency in the left base, that could be caused by a pulmonary embolus.

Figure 1. Posteroanterior roentgenogram of the chest, showing increased heart size and pulmonary congestion.

Doctor Sillman: In regard to the pelvis, this patient was in an automobile accident, several years ago. Dr. Tobin, will you please discuss the case?

Doctor Tobin:* When one reads this case, it seems to be that of an old lady who had had hypertension for years, developed heart failure and renal failure, had a terminal bronchopneumonia, and died of an acute complication, such as a perforated ulcer. But this is too obvious to be Clinicopathologic Conference material. It omits such things as the skin pigmentation, which is mentioned in the protocol

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several times. The patient had stiff elbows—really stiff because she had contractures, meaning trouble for a long time. She had periorbital edema, edema of the scalp, and complained about vertigo. Her sedimentation rate was elevated. She had increased serum globulin, decreased albumin, and she had gastrointestinal symptoms.

Now, in young people we try to fit everything we can into one diagnosis, but in the old, we can often find two or more diseases; however, even in the old, it is good practice to reduce the diagnoses to a minimum. The variety of complaints and the findings which were left out of the first explanation should be fitted in, in some way. To go over them again, we have evidence of disease of the cardiorenal systems, the joints, the blood vessels, the skin, the lungs, and the bowels—a really generalized disease. I believe I can explain all of the symptoms on the basis of one collagen disease.

Collagen diseases are strange. They vary so much in their clinical pictures and each one can involve so many systems of the body that one can't easily sort them out clinically. The group includes periarteritis nodosa, systemic lupus erythematosus, rheumatic fever, rheumatoid arthritis, dermatomyositis, and scleroderma.

The widest variety of symptoms seems to occur in periarteritis and lupus. The two diseases can occur at any age, but periarteritis is much more common in men in the 20- to 40-year-old group. Systemic lupus is likely to occur in women in the 15- to 35-year-old group but both have occurred from infancy to advanced age. These diseases have been known for a long time. I would like to read you a paragraph Osler wrote in 1895 about disseminated lupus erythematosus which in his day was called something a little different.

"By exudative erythema, is understood the disease of unknown etiology with polymorphic skin lesions, hyperemia, edema, and hemorrhagic arthritis occasionally and a variable number of visceral manifestations of which the most important are gastrointestinal crises, endocarditis, pericarditis, acute nephritis, and hemmorrhage from mucosal surfaces. Recurrence is a special feature of the disease and attacks may come on month after month, or even throughout a long period of years. The attacks may not be characterized by skin manifestations."[1]

This description has been gradually amplified. In 1904 the description of frequent joint involvement was noted,[2] as well as pericarditis, pruritus, and kidney disorders, and the constitutional manifestations of fever and prostration. In 1920 leukopenia and thrombocytopenia[3,4] were noted, and in 1924 Libman and Sachs[5] wrote about endocarditis. Nothing more was added until 1935[6] when the wire-loop lesion in the kidney (a hyaline thickening of the glomerular tufts) was described. In 1948 a real contribution was made by Hargraves and associates[7,8] who described the LE cell.

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Now, to get back to this particular case—I can give an equally good argument for periarteritis nodosa or systemic lupus, not the type of periarteritis resembling a hyperallergic response but the type that seems to occur occasionally with hypertension and severe kidney damage. Sometimes one can distinguish these two diseases clinically; the pathologist often has to make the diagnosis. As I told you, periarteritis is more common in men and disseminated lupus is more common in women; for that reason I chose systemic lupus for the diagnosis. The cause of collagen diseases isn't really known. Such things as stress from infection, exposure to sunlight and cold, trauma, and allergic reactions to therapeutic agents like sulfa drugs and penicillin are perhaps not as much a cause as a trigger mechanism which sets off some underlying disturbance that nobody really understands.

This patient had many complaints in the previous two years. When I read them over, it seemed to be the way I also might feel at 73—a case of generalized misery. The brown pigmentation of the arms deserves special notice because in lupus you get, in areas that are exposed to sunlight, reddish, macular lesions such as the familiar butterfly rash on the face. After these lesions heal, a dark pigment remains. This is a spotty affair. In this case pigmentation on the arms, I imagine, was fairly generalized but irregular, leaving certain areas of normal skin, which might be interpreted as vitiligo. She complained of nocturia, which in view of the low specific gravity of the urine indicated loss of concentration and the normal day-night ratio of urine output. The edema of the face, periorbital region, and of the head, is interesting. It is not due to kidney or heart failure—not in the right spot. Her doctor treated it as an allergic disorder and gave her antihistamines. There must have been something about it that suggested urticaria. In collagen diseases, this type of edema might be expected.

Raynaud's phenomenon was experienced by the patient. This occurs in both periarteritis and systemic lupus. The next recurrence that this woman had was characterized by general aching and stiffness. She had a previous history of trouble with her elbows. In lupus about 70 per cent of the people have arthritis. At least once she had normal urine; a second specimen was slightly abnormal, then it became very abnormal. This variation too is found in lupus, which tends to alternately heal and get worse. Her sedimentation rate was high, which relates to the change in albumin-globulin ratio; a finding in lupus too.

Her next difficulty seems to be related to renal failure. Her blood pressure rose and she excreted albumin, and red and white blood cells. She developed a low-grade fever. In this disease, she should have had bouts of fever from time to time. The roentgenogram of the chest, made when she came into the hospital, shows some pulmonary fibrosis and emphysema, and not too great cardiac enlargement. Her history states she remembered hypertension 25 years ago, which was when she was about 50 years old. Women seem to be able to get along with essential

hypertension for years without much deterioration. It is possible, but not very probable, that this hypertension was related to lupus. She should have developed other things in the interval that would fit in with lupus. Lupus is a chronic disease, but I believe hers started 2 or 3 years before, not 25.

Quite a bit of unsuspected pulmonary change can be discovered at autopsy. Nobody pays much attention to this part of the disease because examination of the lungs may reveal a few rales and only little change in the percussion note. There is little evidence of pathology on roentgenograms, and yet the lungs are often involved. These patients do show poor pulmonary function as revealed by function studies. I feel sure this patient will show pathologic changes in the lungs. Many lupus patients have pericarditis or recurrent pleurisy neither of which were seen here. The roentgenograms of the joints don't show changes comparable with her joint symptoms. Hers show osteoporosis, but this can be explained by age. Severe joint changes may occur that look like rheumatoid arthritis but, on the other hand, have very little you can see on a roentgenogram, and yet the patient complains of severe pain and there may be joint swelling.

The patient's urine showed marked changes in the kidney function. She was able to concentrate up to 1.012 and had an elevated blood urea nitrogen. The hemoglobin was reduced; the hematocrit was 31. This was a moderate anemia which would be consistent with this diagnosis. The white blood cell count isn't so consistent. It was elevated. Usually in this disease, leukopenia is present. The electrocardiogram showed nonspecific abnormalities. Myocarditis is another feature of disseminated lupus that may not show much abnormality in an electrocardiogram and still be extensive in the heart. She had no murmurs at all. In Libman-Sachs' disease you are going to get at least a systolic murmur somewhere. I attach no significance to the serum calcium and phosphorus determination.

On the fourth hospital day the patient complained of aching in the maxillary sinus, stomach discomfort. and shortness of breath. I can't explain the sinus pain except on the basis of mucosal edema. Heart-failure patients often have a distended stomach and shortness of breath, and discomfort results. To get back to my favored diagnosis, gastrointestinal symptoms are common in disseminated lupus. The lesion is edema and vascular damage that may progress to ulceration and bleeding into the bowel, and occasionally perforation. One can also get edema of the common duct, ending in pancreatitis.

Something new and sudden happened which precipitated death. She was getting along fairly well when she developed sudden pain, breathlessness, and cold sweats. The pain began at the umbilicus and moved down to the pubis. She improved and had two recurrences—possibly a dissecting aneurysm—the pain moving as it advanced. Or, she, possibly had a ruptured viscus. The trouble with that is that she got along for seven days without showing signs of peritonitis. She was taking

cortisone, which might mask symptoms of a ruptured viscus. Then on the day before she died, she developed a watery diarrhea which was thought to be caused by Terramycin. That could be true, but she had taken antibiotics only six days. It occurs to me that people get diarrhea from antibiotics with a few doses, or after a long period of taking them. This was an in-between period. I think it can be explained as a manifestation of lupus. I do not believe an LE slide was made on this patient. Has anybody a question?

A Physician: Would you say that the roentgenograms are compatible with collagen disease?

Doctor Watts: They are compatible, but not diagnostic.

Doctor Marshall:* I would like to go along with collagen disease. When I was a resident I saw a patient whose illness was very similar to this and which the pathologist diagnosed as scleroderma, so I would like to suggest scleroderma.

Doctor Tobin: Clinically the symptoms of these diseases overlap a great deal. In scleroderma one should have very definite skin changes. The skin gets hard, brawny, waxy and pale. In dermatomyositis you get skin changes, also muscle changes and muscle pain. Because these findings weren't emphasized in the protocol, I chose disseminated lupus.

A Physician: Why do you suppose she had a long history of hypertension?

Doctor Tobin: The easiest explanation is to say it was a labile essential hypertension, not related to her final illness.

Doctor Logan: In reading up on this, I selected three or four diseases—periarteritis, lupus, scleroderma, and dermatomyositis. Scleroderma seemed to fit a little closer than disseminated lupus, so I would like to put in another vote for scleroderma.

Doctor Tobin: I forgot to mention that in scleroderma you can get arthritic changes too.

Doctor Logan: Concerning the terminal event, I thought of ruptured ulcer, particularly in a patient on cortisone, and dissecting aneurysm, but I also would like to vote for mesenteric thrombosis, myocardial infarction, pulmonary embolus, and congestive heart failure.

Doctor Tobin: I interpreted the shadow at the left base as terminal bronchopneumonia rather than pulmonary embolism. The patient should have had, I felt, more symptoms from an embolus. I chose dissecting aneurysm because the pain of perforation of the bowel might have been masked by the cortisone treatment.

A Physician: Don't dissecting aneurysms cause pain in the back?

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*Maj. Charles B. Marshall, USAF (MC), Chief, Aviation Medicine Service.

Doctor Tobin: If they start higher, I think they do. I believe this one started in the abdomen and dissected down.

Dr. Claro's diagnosis:
Arteriolonephrosclerosis

Dr. Tobin's diagnosis:
Disseminated lupus erythematosus

PATHOLOGIC FINDINGS

Doctor Sillman: I think you all did well. This woman had a collagen disease, but it was scleroderma with cardiac fibrosis and pulmonary fibrosis. She had benign nephrosclerosis with superimposed malignant nephrosclerosis. She had a dissecting abdominal aortic aneurysm. Beside that, there was fluid in the chest and abdomen and a few polyps in the large bowel.

Going over the gross autopsy findings rather rapidly, she had a light brown pigmentation that was mentioned. The heart weighed 525 grams and there was evidence of scarring on the gross specimen. Each pleural space contained 800 ml of fluid. The abdomen held 300 ml of fluid. The kidneys weighed approximately 200 grams each and showed some slightly discolorated flecks. The aorta showed dissection extending about 20 cm, but only about 50 ml of blood had actually been extravasated, so this accounted for the pain but in itself did not cause death. The brain was not examined.

Scleroderma is widespread in the body, involving not just the skin but often the heart, lungs, and gastrointestinal tract, as well as muscle, mucous membrane, and kidney. The skin is, however, the classical site. Its pathologic condition can be divided into three stages: the early brawny edema, beginning usually on the extremities, the face, neck or head; the smooth waxy stage; and finally the brown, atrophic, deeply adherent stage. The prodromal symptoms are interesting. Patients frequently have the weakness and fatigue of which this woman complained, sometimes weight loss, occasionally fever, joint pains, or joint stiffness. Raynaud's phenomenon is quite common as a prodrome in scleroderma. In one group of 15 patients, 12 of them had Raynaud's phenomenon. There is loss of hair and pruritus. Cardiorespiratory symptoms are not too rare. They may be early before you see anything diagnostic. The patients may have heart murmurs and enlarged hearts, rales, and electrocardiograms with nonspecific changes.

The laboratory findings are not particularly diagnostic. A mild anemia, elevated sedimentation rate, and sometimes reversal of the albumin-globulin ratio. The urine, as in this case, shows red and white blood cells, and casts. Roentgenographic studies may reveal osteoporosis, as in this patient, or gastrointestinal tract involvement, which was not present in this case, and often linear or nodular markings in the lung. Fifty per cent of the patients in one series showed these lung changes.

The slides in this case showed, first, some edema of the skin, with dense collagen fibers (fig. 2). The dermis is fairly solid with fibrotic tissue, and the epidermis is markedly atrophied (fig. 3). The skin appendages are sparse except for sweat glands. For some reason they seem to remain. Looking at the epidermis a little closer one can see that the dermal papillae are still there; in severe cases the papillae flatten out, but one doesn't see skin appendages very often in this slide.

We have no slides of the gastrointestinal tract there. If it is involved, symptoms such as difficulty in swallowing, nausea, vomiting, and diarrhea or constipation may occur. The usual finding in the heart is fibrosis. This patient had a small amount of fibrosis. The lung can show fibrosis, with or without cystic changes. The alveolar walls of the lung in this patient are thickened, not markedly so, but probably enough to explain her symptoms.

The kidney changes are interesting. A scleroderma kidney has been described that is so like malignant nephrosclerosis, it is difficult to tell them apart. The only difference reported is the thickening of the arterioles, which show a gelatinous or mucoid change. This is a very rare finding in a rare disease. The kidney in this patient shows thickening of the arterioles, fibrinoid degeneration of the afferent arterioles, and hyaline changes. Here is a classical glomerulus (fig. 4) showing the changes of malignant nephrosclerosis with fibrinoid change involving an efferent arteriole going into the glomerular arterioles, as also described in a scleroderma kidney. The pancreas and spleen showed some fibrinoid changes in the arterioles.

In scleroderma a certain percentage of patients get malignant hypertension—about 3 out of 10. These become uremic in a very short time. It had been suggested that treatment with ACTH and cortisone precipitated the malignant phase. Inasmuch as it occurs suddenly anyway, this is still theory. In scleroderma, death is usually a result of intercurrent infection because the patient becomes weak and emaciated. When the patient develops severe hypertension, the causes of death are similar to those of malignant hypertension, a cerebrovascular accident, heart failure, or uremia. In this patient there also was a small pulmonary embolus on the left side which had not caused an infarct.

As the brain was not examined, we can only speculate on the cause of death. The dissecting aneurysm could have contributed to the renal damage by a period of shock. There may have been some uremia, but this cannot be proved as there was no recent determination of blood urea nitrogen. There was heart failure as indicated, among other things, by the large amount of pleural fluid, and there may have been cerebral changes. Are there any questions?

Doctor Green:* What about the bowels?

*Maj. Harry C. Green, Jr., USAF (MC), Chief, Surgical Service.

Figure 2. High-power view of dermis from right center portion of the section in figure 3, showing dense collagenous fibers. (× 525)

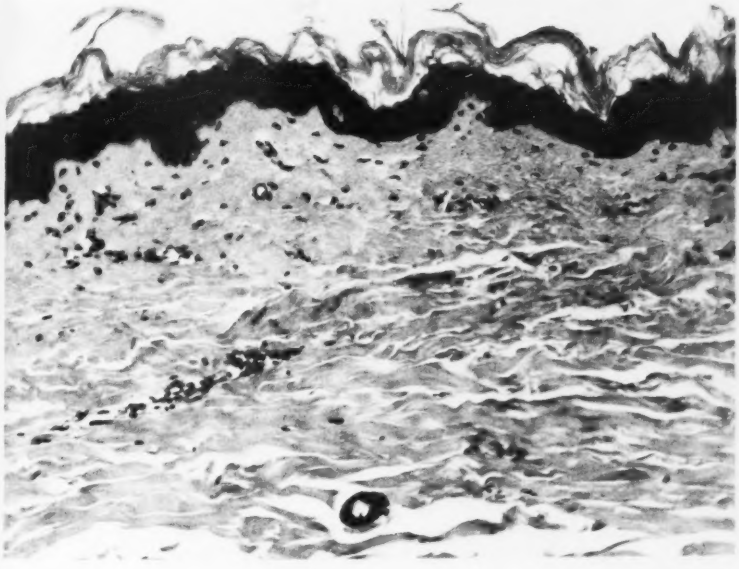

Figure 3. Section of skin showing dense collagenous fibers, fibrotic tissue, and atrophy of epidermis. (× 195)

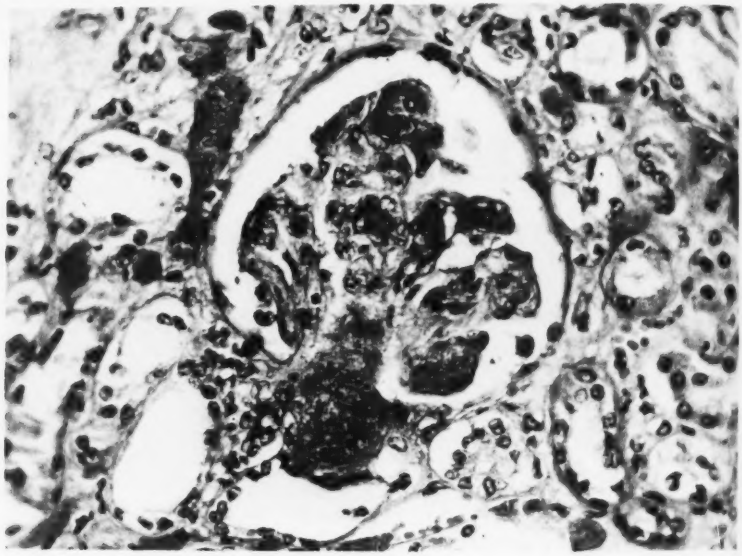

Figure 4. Section of kidney showing fibrinoid degeneration of afferent arteriole extending into glomerular capillary. (x 305)

Doctor Sillman: The bowel showed nothing unusual. It was examined carefully. There was no unusual amount of fibrosis, at least in the areas of which we have sections.

Pathologic diagnoses:

1. Scleroderma, with cardiac and pulmonary fibrosis
2. Nephrosclerosis, benign, with superimposed malignant nephrosclerosis
3. Dissecting abdominal aortic aneurysm

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SERVICE ARTICLE

THE BASIS OF EFFECTIVE VECTOR CONTROL

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OBJECTIVE self-appraisal is one of the least traveled pathways to progress, and yet, organizations as well as individuals may experience some stimulation for improvement by a "look in the mirror." This is particularly true of that part of the post preventive-medicine program which deals with insects and rodents as vectors of disease. A military installation with conditions that allow insects to breed freely is a mirror that reflects apathy toward the disease potential inherent in large populations of flies and mosquitoes.

In a military organization, a sentry found sleeping on watch merits the court-martial that usually ensues. Apathy toward a disease noted for its prolonged absence in epidemic proportions is similarly dangerous, even though an "at ease" posture may seem justified. Unfortunately, diseases transmitted by arthropods are characterized by a tendency to promote such apathy.

As late as 1947 there were more than 50,000 deaths in one Indian state from plague alone. In continental United States during the years 1952-1956, the median annual number of cases of malaria was 715. In 1957, up to 20 July, there were 66 cases of endemic typhus and 823 cases of infectious encephalitis.[2] Among military personnel in the Fifth U. S. Army Area during 1956 there were at least 5 cases of tularemia, as evidenced serologically by increased titers; and in 1957 there were several additional cases, one of which has been definitely associated with the bite of a tick.[3] These occurrences lend substance to the very real disease potential presented by arthropod vectors.

BASIC CONSIDERATIONS

There are some basic considerations of utmost importance in the vector control program which must be oriented properly. They should be viewed with a perspective that takes into account the array of problems confronting the Post Commander, the Post Surgeon, and the Post Engineer.

Recognition of Problem. Recognizing that an actual or potential breeding site for insects and rodents does exist is the first mark

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of progress in vector control. Realistically, there are obstacles in the form of financing, manpower shortages, and equipment inadequacies that make progress difficult. The insect and rodent control program, however, should not be an isolated endeavor standing apart from all other post activities. It should be an integral part of planning, so that various phases of beautification and maintenance may accomplish the aims of preventive medicine, which then becomes an adjunct to esthetics and economy. Chandler[4] quoted M. C. Hall as saying, "the louse had its welfare imperiled when the Saturday night bath supplanted occasional immersion from falling into water. . . . The housefly got a severe setback when the automobile replaced the horse." It would be ridiculous to suppose that these two social innovations were instituted for the control of the louse and the housefly, but the effect was the same. The tools of preventive medicine are often found under guise, and the ability to recognize fortuitous circumstances as allies and to enlist them in the cause is the mark of an experienced Preventive Medicine Officer.

Importance of Basic Sanitation. The results of the use of DDT for the control of typhus in Naples in 1943-1944 were dramatic, but not without perverse effect. To many, the advent of DDT and related insecticides heralded a new era in the realm of insect control; however, past experience as well as recent investigations furnish substantial evidence that basic sanitation will never yield to chemicals its rightful position in the control of disease vectors. In certain situations it appears that flies are capable of producing more offspring in the presence of larvicides than where no chemicals have been applied,[5] and the development of resistance to insecticides may be accelerated or augmented by larvicides.[6] Nothing is changed on a permanent basis by the use of chemicals as a control measure, whereas application of the principles of practical ecology (*i. e.,* filling ponds where mosquitoes are breeding and clearing debris from drainage ditches) proves not only more effective but obviates any need for repetition. Good housekeeping practices are still the first line of defense against insect pests and vectors.

Control With Chemicals. Chemicals play an important role in the control of vectors, but must be secondary to the methods mentioned above. The effectiveness of chemical control is largely dependent on application technics. These may be made more efficient by selective use of the chemical, based on a knowledge of breeding habits and life histories.

Identification of Vectors. An effective control program is contingent on the collection and identification of insect and rodent vectors. The direction of the attack is dictated by the information on life history that is corollary to identification. Army medical laboratories are prepared to identify specimens, and specific

instructions concerned with collection and shipment of insects are furnished by each laboratory.

Community Education. Perhaps no other field of medical endeavor so involves lay participation as does preventive medicine. Each member of the Armed Forces and his dependents should be conscious of their role in the prevention of disease in the community. Various educational media may be employed in appraising them of their responsibilities. Community education completes the fundamental triad of good housekeeping, chemical control, and an informed public.

Co-ordination. The Post Surgeon and the Post Engineer are the Post Commander's right and left hands. In this situation it is imperative that the right hand should know what the left hand is doing. Close co-ordination between the Post Engineer and the Post Surgeon is essential if progressive steps are to be made toward producing a vector-free environment for troops and dependents.

In all of these considerations, individual responsibilities are only inferred, but most military personnel are aware of specific regulations defining responsibilities that pertain to them individually. Many are the instances where there is a wide gulf between knowing responsibilities and having the wherewithal to accomplish the mission. The support of the Commanding Officer in designating a cleanup day could be a useful tool in this instance. A maximum effort in manpower and equipment directed toward the clearance of unsightly or undesirable conditions on the post would lend great support to the engineer maintenance program while reducing insect and rodent breeding areas. Other types of "do-it-yourself" projects, well organized on a company or battalion level, could produce some very worthwhile results.

SUMMARY

Critical appraisal of the post vector-control program at frequent intervals is essential in view of the dangerous apathy likely to prevail. Effective control depends on (1) integrating the control program into post beautification and maintenance activities; (2) directing the major effort toward basic sanitation and good housekeeping measures, especially those having a permanent effect; (3) using chemical control only as secondary to basic sanitation; (4) collecting and identifying all vectors, and directing attack in accordance with breeding habits and life histories; (5) educating military personnel and dependents as to their responsibility in the control program; and (6) obtaining both the support of the Post Commander and co-ordinated action by the Post Surgeon and Post Engineer.

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MISSILE TYPE INJURIES FROM ROTARY LAWNMOWERS

"The introduction of any mechanical, labor-saving device into routine life may hold unsuspected danger for its users. In recent years the efficiency of the rotary power lawnmower has been recognized widely. This mower has enjoyed increasing sales and popularity, and its use is now quite commonplace.... Direct contact with the rotary blade most often results in damage to the fingers, hand, toes, or feet.... However, practically no mention has been made of a more sinister injury which has been encountered since the advent of the rotary power lawnmower. This type of injury is caused by some object being hurled through the air by the rotating blade of the mower. Examination of a rotary lawnmower in action discloses that there is usually a certain amount of debris thrown from under the cowling which houses the blade of the mower. Unevenness of ground or inadequate protection by this shield allows debris thrown by the blade to travel freely through considerable distances. Objects such as glass, steel, wire, stones, or aluminum lying on a lawn can be accelerated rapidly to high speeds making them similar to war missiles. The force applied to these flung objects must be great judging from the injuries received. In most instances the victims of these injuries have been bystanders who were not operating the lawnmower. This particular missile type of injury is peculiar to the rotary type lawnmower and is not characteristic of the conventional power lawnmower."

—GEORGE R. MILLER, M. D.
in *Southern Medical Journal*
pp. 982-983, Aug. 1957

Dermatomyositis Associated With Pregnancy

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THE purpose of this article is to call attention to the difficult problem of differential diagnosis of the collagen diseases by presenting a patient with dermatomyositis, and to discuss the effects of the association of pregnancy with this disease.

CASE REPORT

A 27-year-old Caucasian woman was first seen on 6 February 1956. At that time she had a pruritic, diffusely erythematous facial lesion with butterfly distribution, of two months' duration. There was no photosensitivity, and she was otherwise asymptomatic. Differential diagnosis included seborrheic dermatitis, acne rosacea, and lupus erythematosus (LE). One LE preparation was negative. She was treated with lotio alba.

First Hospitalization

On 28 March the patient was hospitalized because of right costovertebral angle and right upper quadrant tenderness. She had an upper respiratory infection one week prior to admission, and experienced frequency without dysuria or hematuria. Her skin eruption persisted.

Physical examination. Vital signs were normal. The rash was unchanged. Tenderness was as described. The remainder of the examination was unremarkable.

Laboratory examination. Red blood cell count was 3.9 million per μl, hemoglobin was 12 grams per 100 ml, and white cell count was 6,000 per μl, with a normal differential. Sedimentation rate was 22 mm/hour (corrected). Urinalysis was normal except for a few red and white blood cells on several occasions. Prothrombin time was normal. Bromsulphalein retention (BSP) was less than 5 per cent. Heterophil agglutination was negative. Total protein was 6.9 grams per 100 ml with an albumin of 4.4 grams per 100 ml. Bilirubin was less than 1.0 mg per 100 ml. Cephalin flocculation test was negative. Six LE preparations were negative. Roentgenograms of chest and abdomen were normal. An intravenous pyelogram was negative.

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Hospital course. The patient was treated with Gantrisin (brand of sulfisoxazole) for her urinary complaints and Selsun (brand of selenium sulfide) shampoos for seborrheic scalp changes. An internal medicine consultant advised a high suspicion for collagen disease. She was discharged, symptomatically improved, after two weeks.

Second Hospitalization

Because of a 15-pound weight loss over the preceding four months, the patient was rehospitalized on 10 May. Right upper quadrant tenderness had recurred immediately following her hospital discharge, but she had remained afebrile.

Physical examination. Vital signs were normal. Fine scaling of the erythematous facial rash was noted; there was no atrophy. Right sided costovertebral angle and upper abdominal tenderness were present. A posterior-wall fibroid tumor of the uterus was palpated. Physical examination was otherwise normal.

Laboratory examination. A complete blood count was unchanged. Sedimentation rate was 32 mm/hour (corrected). Urinalysis was normal, as were 20 LE preparations. Liver function studies revealed the following: BSP, 17.5 per cent retention; bilirubin, 1.5 mg per 100 ml, with a direct fraction of 0.7 mg per 100 ml; cephalin flocculation, 2 plus in 24 hours and 3 plus in 48 hours; thymol turbidity, 4 units; total protein, 7.6 grams per 100 ml, with 4.4 grams albumin per 100 ml. A trichinella skin test was positive. An electrocardiogram (ECG) was normal. Serology was negative. Roentgenograms of gallbladder, colon, stomach, and small bowel were normal except for a suggestion of hepatomegaly.

Hospital course. A gynecological consultant concurred in the diagnosis of uterine fibroid tumor, and advised no therapy. Right upper quadrant pain persisted, and on the tenth hospital day the muscles of both upper arms became painful and tender. An internal medicine consultant advised biopsies of liver, skin, and deltoid muscle.

A repeat blood count revealed 10 per cent eosinophils. Repeat liver chemistries showed a normal BSP, and a cephalin flocculation of 1 plus in 24 and 48 hours; other values were unchanged.

Because of the suspicion of collagen disease, a trial of Meticorten (brand of prednisone) was begun. On 40 mg per day there was symptomatic improvement in four days.

The liver biopsy was normal; the skin biopsy showed chronic dermatitis, but no evidence of collagen disease. The muscle biopsy was interpreted as "acute myositis, with severe necrosis, consistent with dermatomyositis." The Armed Forces Institute of Pathology concurred in these interpretations (fig. 1).

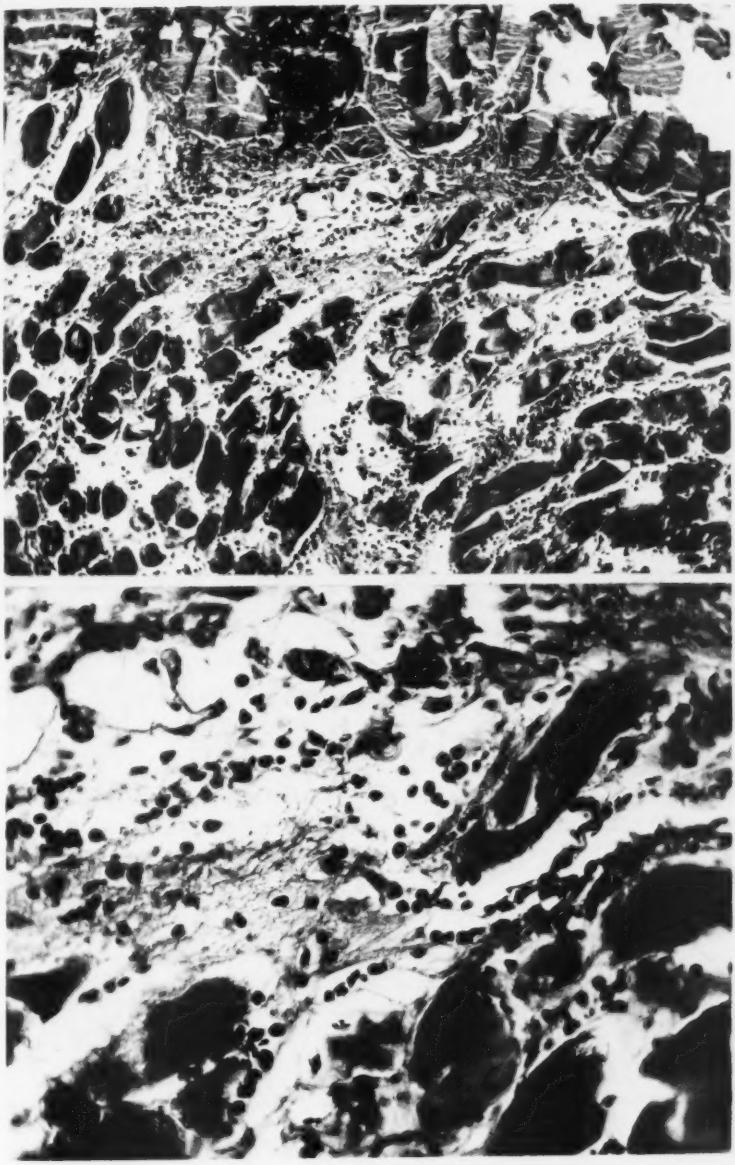

Figure 1. Photomicrograph of section from muscle biopsy showing acute myositis with severe necrosis. (Above, × 100; below, × 300)

A recurrence of muscle pain required an elevation of the dose of Meticorten to 50 mg per day, and on this therapy there was progressive improvement. The deltoids, biceps, and triceps were noted to be soft, with some limitation of movement. Transient tenderness of both gastrocnemius muscles occurred. The 24-hour urinary creatinine was 1.2 grams, and creatine was 0.4 gram (elevated).

The patient was discharged, improved, on 8 May.

Third Hospitalization and Subsequent Course

One week later, while on 50 mg Meticorten, severe muscle pain recurred in all extremities. The patient was rehospitalized, the Meticorten was raised to 60 mg, and testosterone, 25 mg twice a week, was added. She improved rapidly, was discharged in one week, and has not again been hospitalized for her dermatomyositis, inasmuch as her symptoms have been maintained under control except for minor flare-ups, especially noted after minor infections.

The testosterone was discontinued about one month after it was started, because symptoms had subsided and the patient had developed a severe case of acne vulgaris. The dosage of the Meticorten was gradually decreased by about 5 mg per week. An attempt was made to discontinue it, but symptoms recurred, and a maintenance dosage of 25 mg per day was finally found to be the lowest amount that would keep her symptom-free.

In addition to the Meticorten, maintenance therapy included KCl in doses up to 4 grams per day, a low salt diet, and 25 units of ACTH intramuscularly every other week. Biweekly blood pressure determinations, weight measurements, and urinalyses, and monthly fasting blood sugar determinations were made. A physical examination was done weekly.

The patient became pregnant in August. Toward the end of the first trimester she developed pyelitis. *Escherichia coli* was cultured from the urine. She was treated with Gantrisin and symptoms subsided. There was no recurrence.

The frequency of minor flare-ups of symptoms became gradually less during the course of the pregnancy, and it was found that the maintenance dose of the Meticorten could be lowered to 20 mg per day with no untoward reaction.

This was the patient's second pregnancy. She had had no abortions. The first pregnancy had resulted in a normal, spontaneous, full-term delivery. The child was living and well, and about 3 years of age.

Obstetrical examination was normal, and revealed an adequate pelvis. During the course of the pregnancy, the patient was treated as any other prenatal patient, except that routine prenatal checks were made every week in conjunction with her medical examination. There were

no complications until the early part of May 1957, about two weeks prior to her estimated date of confinement, when she presented with rather copious vaginal bleeding and irregular, weak uterine contractions.

Fourth Hospitalization

On admission, the hemoglobin was found to be 7 grams per 100 ml. By the time the consultant in obsetrics arrived, the contractions had ceased, but the bleeding continued. The cervix was thick, soft, and dilated about 2 cm. Blood was issuing from the os in moderate amounts. The fetal head was not felt to be engaged. There was no tactile evidence for the existence of a placenta previa. The fetal heart rate was 150 and regular.

Within an hour the bleeding stopped. There were no contractions. The fetal heart tones remained good. The patient's hemoglobin rose to 11 grams per 100 ml following transfusion with two pints of blood. She was observed on the obstetrical ward for several days. There was no further bleeding and she was discharged after four days.

Fifth Hospitalization

The patient was again admitted to the obstetrical ward during the first week in June, because of moderate contractions every five minutes and a rather heavy bloody show. The fetal heart was regular and of normal rate. After a labor of about six hours, the patient spontaneously delivered a seven-pound infant who appeared normal in all respects. Examination of the placenta revealed a marginal sinus rupture.

The patient was discharged on the fourth post-partum day. Post-partum course had been normal. The baby did well on a routine regimen.

Following delivery the patient's Meticorten was raised to 30 mg daily, and then gradually reduced in accordance with the scheme mentioned previously. This was done to obviate a possible recurrence of symptoms of the dermatomyositis in the post-partum period because of hormonal change.

DISCUSSION

Dermatomyositis is an acute, subacute, or chronic disease that involves the skin, subcutaneous tissue, and skeletal muscle.[1] It is of unkown etiology, and is grouped with the collagen diseases.

Clinically, the major findings are tenderness and pain over skeletal muscle, particularly of the extremities, and a non-specific dermatitis that has certain typical characteristics. Other findings are those which may be found in the other systemic collagen diseases. Creatinuria is a constant finding, and there is a high incidence of eosinophilia.

The onset is commonly noted to follow an upper respiratory infection. The disease may be accompanied by a low grade fever.

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There is no sex predisposition. The victims tend to be children or young adults.[2] The presenting symptom may be myositis, dermatitis, or any of the systemic manifestations of collagen disease. It has been noted that about 25 per cent of patients with dermatomyositis develop or have neoplastic disease. The relationship is not understood.[3]

The mortality rate in acute dermatomyositis is about 50 per cent.[3] The majority of the remaining patients go on to follow a chronic recurrent course that may go on for years, and eventually terminates in death. A small percentage recover from the acute episode and never have a recurrence.

Lupus erythematosus, scleroderma, dermatomyositis, and periarteritis nodosa constitute the collagen diseases. These four entities were first grouped together by Banks[4] in 1941. There is little doubt that the collagen diseases belong together. The question is whether they are really separate entities or part of a single clinicopathologic continuum. There is a good deal of evidence to support the latter view. Talbott[5] states that dermatomyositis may be indistinguishable from acute lupus erythematosus clinically, and indistinguishable from scleroderma pathologically. Scleroderma, proven pathologically, has been reported with positive LE preparations. Sclerodermatomyositis is being recognized as an entity.[6]

In discussing the differential diagnosis of these diseases, the above facts should be kept in mind. The "typical" findings in each of these conditions may not be the usual, and a confusing mixture may present itself.

On the skin, in lupus, discoid variety, one sees a classic triad consisting of telangiectasia, atrophy, and follicular plugging. In the acute form, this classic triad usually does not have time to appear, and one sees diffuse erythema with fine adherent scaling, especially in the so-called butterfly area. In scleroderma, the skin is thin and bound down, as well as atrophic. Pigmentary changes occur in all the collagen diseases. This is secondary to epidermal injury.

The eruption in dermatomyositis classically starts with erythema and edema of the face, particularly in the butterfly area and about the eyes. There may or may not be atrophy. In a series of 25 cases, Sheard[7] reported "rash on the face or swollen eyelids" as the presenting symptom in 32 per cent of the cases. If, however, a patient is seen with odd multiple eruptions or generalized eruption that remind one of collagen disease but are not really typical of anything, and especially if the patient is complaining of muscular weakness or tenderness, then dermatomyositis should be considered.

The clinical manifestations in collagen disease include dermatitis, involvement of serous and synovial membranes (polyserositis and polyarthritis), evidence of vascular changes (kidney, retina, nodules), fever, and moderate anemia. The presence of these manifestations should make one think of collagen disease.

From the laboratory standpoint, the sedimentation rate may be elevated and there may be leukopenia. The A/G ratio may be reversed. Lupus is frequently accompanied by a thrombopenia and a false positive serology. Subcutaneous nodules along the course of a blood vessel occur in periarteritis; in this condition the trichinella skin test frequently is positive. Specific findings in dermatomyositis have already been discussed.

Histologically, acute lupus is distinctive, with epidermal atrophy, liquefaction necrosis of the basal layer, and fibrinoid degeneration of the corium. In periarteritis one sees an obliterating panarteritis. In scleroderma, the typical findings are thinning and atrophy of the epidermis with obliteration of the appendicular structures and rete ridges, and massive homogenization of the collagen in the corium. In dermatomyositis, one usually finds a necrotizing myositis and findings consistent with chronic dermatitis. Occasionally findings closely resemble scleroderma.

Therapy

Until the advent of steroid therapy, treatment of the collagen diseases was entirely unsatisfactory. Cortisone, in the skin and subcutaneous tissues, acts primarily as an anti-inflammatory agent. It delays the normal inflammatory response even if a stimulus is present. The exact site of action is still controversial, but it seems certain that the drug directly affects the vascular bed and at the same time slows or prevents fibroblastic activity. This would explain the effectiveness of the drug in collagen disease.

In treating any disease with parenteral steroids, the most effective regimen consists of starting with high doses (50-100 mg daily of Meticorten, or the equivalent in cortisone, hydrocortisone, or ACTH), and then gradually decreasing the dosage to maintenance levels that are arrived at by trial and error. If the initial dosage is too low, the patient's disease may escape control and increasing dosages may be of no avail.

Complications of steroid therapy occur, and precautions must be taken. Frequent physical examinations should be made. KCl to prevent hypokalemia and a low salt diet to prevent hypernatremia are essential. Periodic checks for hypertension, weight gain, glycosuria, and hyperglycemia should be done. Periodic

electrocardiograms are indicated. Any evidence of concurrent infection should be vigorously handled with high doses of antibiotics to prevent dissemination. Personality changes should be watched for. The patient should be told to inform the doctor immediately of any tarry stools or abdominal pain.

The results of steroid therapy in collagen disease have not been consistently good. This is true in dermatomyositis. McElligott[8] stated that the steroids are more effective in the acute cases and usually fail to improve the chronic cases. He went on to say that the drugs should not be withheld from these people, however, because there have been some reported successes. Lamb and Jones[9] believed that the steroids should rarely be used in dermatomyositis, claiming that they are only effective in about 20 per cent of cases. They preferred testosterone as the therapy of choice. The rationale for this is that since dermatomyositis is a necrotizing myositis primarily, the anabolic effects of testosterone should aid considerably in preventing muscular destruction.

Dermatomyositis and Pregnancy

There is no reference to dermatomyositis with accompanying pregnancy in the recent literature. Andrews[6] describes a case of sclerodermatomyositis that started after childbirth. There have been reports in the literature of scleroderma and lupus with pregnancy.[10] The concensus is that the disease either improves or is not affected by the pregnancy. This is ascribed to increased output, in pregnancy, of steroids and steroid-like hormones. This point is still controversial. It appears that there is an increased rate of abortion in patients with collagen disease.

Our patient was followed for almost two years. It was our impression that a clinical remission took place during the pregnancy. Objectively, we found that we could lower the dose of the steroid. In coming to this conclusion it must be borne in mind that spontaneous remissions in dermatomyositis do occur. We were concerned with the possible effects of the drug on the infant. There were none. The child was perfectly normal. We also were concerned with the possibility of a flare of the dermatomyositis during the post-partum period. We therefore increased the dose of Meticorten immediately following delivery, and then gradually returned to a maintenance dose. No flare-up of symptoms was noted.

SUMMARY

A case of dermatomyositis associated with pregnancy has been presented, with emphasis on the differential diagnosis of collagen disease, and the effects of pregnancy on collagen disease.

This patient was treated with Meticorten, ACTH, and testosterone. She delivered a normal, full-term infant. There appeared to have been a remission during the pregnancy. There was no post-partum flare.

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CORONARY ARTERY DISEASE AS REPORTED CAUSE OF DEATH

"The publicity given to the rise in coronary artery disease has of itself led to greater awareness of the disease. As a result, an increasing number of deaths are being reported as due to coronary disease by coroners and medical examiners where the deceased had not received medical attention or the cause of death was not known. In one area of the country, more than 35 per cent of the deaths reported as coronary disease were certified by the medical examiner's office. In New York City in December 1956 some 15 percent of the deaths from arteriosclerotic heart disease and 44 percent of the deaths attributed to coronary artery disease were medical examiners' cases. Only a very small proportion (4 percent and 9 percent, respectively) of these diagnoses were verified by autopsy."

—*Statistical Bulletin*
Metropolitan Life Insurance Co.
p. 3, Feb. 1957

Hepatic Cirrhosis Mistaken for Lupus Erythematosus in a Young Girl

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IN 1956, Bearn, Kunkel, and Slater[1] reported 26 cases of severe hepatic cirrhosis of undetermined cause in young women. Ethanol, nutritional deficiency, and viral hepatitis were excluded as etiologic agents in their series. Our case falls in the same category, and is thought to be important in that there was an apparent involvement of multiple systems. Because of this apparent involvement, a mistaken diagnosis of lupus erythematosus was made originally.

CASE REPORT

The patient was a 14-year-old Caucasian girl who was first hospitalized on 4 August 1956 because of bilateral ankle edema. During the previous year she had had frequent epistaxis, a nonproductive cough, and fatigue, all of which were aggravated by exercise. Three months before her admission to the hospital, she was seen by a physician for persistent orbital headache and suffusion of the conjunctiva. No significant abnormalities were found, and these complaints subsided spontaneously. Two months before admission she had had an unusually severe nosebleed that lasted two days. This was followed by a temperature of 102°F, abdominal pain, and diarrhea lasting 24 hours. At this time there was pain in the muscles of both legs which interfered with ordinary activity and at times was associated with localized edema.

Periorbital edema was present each morning on arising, and persisted for two or three hours. The edema continued to recur until just before the patient's admittance to this hospital. One month before this admission she noticed a marked increase in fatigue and swelling of one leg that persisted for two days. One week before hospitalization she complained of dizziness and diarrhea, and had a temperature of 102.2°F. She was treated for gastroenteritis, and the symptoms sub-

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sided after one day. On 3 August she had bilateral ankle edema and was hospitalized the following day.

As an infant, the patient had had pneumonia and bronchitis, as well as the common acute exanthemas of childhood. She denied having had scarlet fever or rheumatic fever, either by name or by symptoms, and there had been no jaundice beyond the neonatal period. The menarche had occurred six months prior to her admission and was followed by amenorrhea.

The patient was well nourished, well developed, and did not appear ill. Her height was 67 inches; weight, 120 pounds; temperature, 98°F; pulse rate, 88 per min.; respiration, 20; and blood pressure 128/80 mm Hg. She had no rash, but there was 1 plus pitting edema of her ankles bilaterally. Her head, eyes, and ears were normal. Her nose showed only increased vascularity of the mucous membrane. The remainder of the physical examination was normal except for the abdomen, where a firm, nontender mass was noted in the left upper quadrant, extending 5 cm below the costal margin. The mass was thought to be the spleen, and on intravenous pyelography it could be seen displacing the left kidney downward.

Initial urinalysis revealed a specific gravity of 1.030, and 2 plus proteinuria. Numerous erythrocytes and granular casts were noted in each high-power field. Subsequent specimens of urine were unchanged except that erythrocytes and casts were noted only on one other occasion. Blood studies showed a leukocyte count of 4,000 per μl with 58 per cent neutrophils and 42 per cent lymphocytes. Hemoglobin was 13 grams per 100 ml; hematocrit, 35 ml per 100 ml; and the sedimentation rate, 19 mm per hour (Wintrobe). Prothrombin, bleeding, coagulation, and clot retraction times were normal. Serologic tests for syphilis were consistently negative. Blood urea nitrogen was 15 mg per 100 ml. Total serum cholesterol was 126 mg per 100 ml, with ester fraction of 31 per cent. Total serum protein was 5.0 (albumin, 2.14; alpha globulin, 0.61; and beta globulin 2.25) grams per 100 ml. C-reactive protein and antistreptolysin titers were negative. No lupus erythematosus (LE) cells or allied phenomena were found on repeated examination. The thymol turbidity was 12.8 units; cephalin-cholesterol flocculation, 4 plus in 24 hours; and there was 31 per cent retention of Bromsulphalein 45 minutes after intravenous injection of 5 mg per kg of body weight.

During her initial hospitalization the patient had had several minor episodes of epistaxis, which were easily controlled. Aside from this she had no complaints, and after 33 days in the hospital she was discharged with a presumptive clinical diagnosis of a diffuse collagen disease. Three days later she was readmitted because of further epistaxis, marked malaise, fatigue, and pain and tenderness in the left calf.

On this admission the leukocyte count was 3,300 per μl, with a differential count of 47 per cent neutrophils, 12 per cent eosinophils,

1 per cent basophils, 36 per cent lymphocytes, and 4 per cent monocytes. A few target cells and spherocytes were noted, and the platelets appeared to be slightly decreased. A serologic test for syphilis was negative. Total serum bilirubin was 1.32 mg per 100 ml, with a direct bilirubin of 0.24 mg per 100 ml. The Bromsulphalein test showed 40 per cent retention at the end of 45 minutes. Thymol turbidity was 15.7 units, and cephalin-cholesterol flocculation was 4 plus in 48 hours. Prothrombin time was normal on entry, but fell to 63 per cent activity while the patient was in the hospital. LE preparations were consistently negative.

In spite of abnormal findings in the liver-function tests, it still was believed that the patient had lupus erythematosus or, less likely, polyarteritis nodosa, because of symptoms and laboratory findings suggesting multiple-system involvement and the lack of physical evidence of hepatic disease. A muscle biopsy from a tender site in the left calf was normal. Bone marrow aspiration showed a normal cellular marrow.

Needle biopsy of the liver was attempted twice without success. On the first attempt, sedation was accomplished with 100 mg of pentobarbital sodium and 50 mg of meperidine hydrochloride. Following this medication the patient was drowsy and somewhat confused for two days, which apparently was due to the medication, as no untoward effect was noted from the biopsy itself.

During the second hospital course, intermittent pain in the left upper quadrant became a serious problem. Two-milligram doses of dihydromorphinone hydrochloride were required for relief of pain. This drug produced no untoward effect. Examination disclosed only an enlarged tender spleen. Repeat leukocyte counts were unchanged, showing a slight leukopenia with a normal differential count. During her third hospital week, the patient had a temperature of 102°F, with nausea, vomiting and constant left upper quadrant pain, but no significant changes were noted either on physical or laboratory examination. She was treated symptomatically, and after three days the symptoms began to clear. After one week, only the inconstant pain in the left upper quadrant remained. After 32 days the patient was again discharged to her home, symptomatically improved and with a diagnosis of probable lupus erythematosus.

After leaving the hospital the patient had a low-grade fever, marked weakness, and more frequent epistaxis. She was admitted on 26 October for the third time, only three weeks after discharge. Physical examination revealed no new findings. The hemogram was essentially unchanged; the platelets numbered 152,000 per μl. Urinalysis showed 2 plus albumin, 2 to 4 granular casts, with an occasional erythrocyte or leukocyte per high-power field. Serum alkaline phosphatase was 10.8 Bodansky units; total serum cholesterol was 232 mg per 100 ml, with ester fraction of 68 per cent and, on 27 October, the total serum

protein was 5.43 (albumin, 3.28) grams per 100 ml. Repeat LE preparations were negative. Prothrombin ranged from 50 to 70 per cent activity, and was not affected by vitamin K_1 oxide. Maximal postoperative serum bilirubin, was 14.0 mg per 100 ml, with a direct bilirubin of 7.0 mg per 100 ml. Thymol turbidity was 16.7 units, and cephalin-cholesterol flocculation was 4 plus in 48 hours. Bromsulphalein retention was 43.8 per cent at 45 minutes.

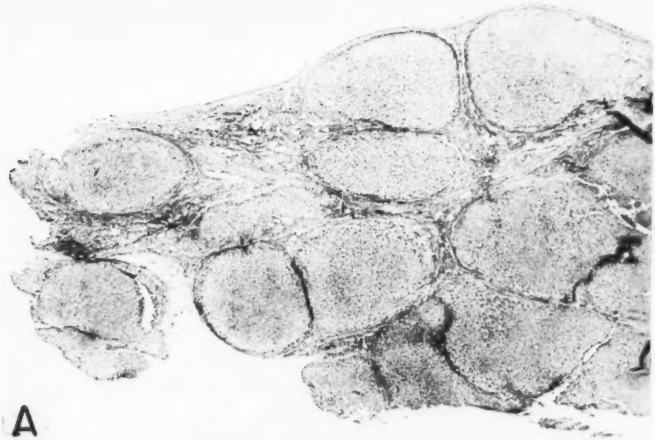
The original diagnosis of a diffuse collagen disease now seemed unlikely in view of the persistently negative LE preparations and the negative muscle biopsy. The timely article by Bearn, Kunkel, and Slater[1] on hepatic cirrhosis of obscure cause revealed a striking similarity between this patient and those they described. Roentgenographic examination of the upper gastrointestinal tract failed to show any evidence of esophageal varices. The only abnormality noted was a pressure defect of the stomach as a result of the large spleen. The liver shadow appeared small.

On 13 November an exploratory laparotomy was done to confirm the diagnosis of hepatic cirrhosis and to perform a portacaval shunt if warranted. When the liver was visualized, its total size was only about one third to one half the normal size. It was hard and the surface was studded with small nodules of regenerating liver tissue. The spleen was smooth and firm, and was two to three times the normal size. The appearance of the mesenteric veins did not suggest an increased portal pressure. By direct measurement, however, the pressure in the portal vein was found to be 250 mm of water. The appearance of the liver indicated far-advanced cirrhosis, with a very poor prognosis. It therefore was decided that a portacaval shunt was not indicated, but a liver biopsy was performed.

The specimen showed the architectural pattern distorted by heavy bands of connective tissue, which surrounded lobules to form nodules from 2 to 3 mm in diameter. Many of the lobules showed intact central veins with preservation of the surrounding liver cells. The separating connective tissue septums contained increased numbers of rudimentary bile ducts and a diffuse infiltration with lymphocytes, neutrophils, and a few eosinophils. The presence of numerous portal canals, which were either within normal limits or only slightly altered and which did not enter into the formation of pseudolobules, met the criteria for the diagnosis of postnecrotic cirrhosis (fig. 1).

The patient's immediate postoperative course was uneventful except for a gradual increase in the serum bilirubin. Three weeks after surgical intervention there was a sudden sharp increase in the serum bilirubin, associated with the appearance of ascites and accompanied by anorexia and marked weakness. The patient was treated with a low-salt diet and chlortetracycline hydrochloride (aureomycin) with only minimal improvement.

Because of the critical nature of her disease, it was her parents' desire that the patient return to the United States. She therefore was



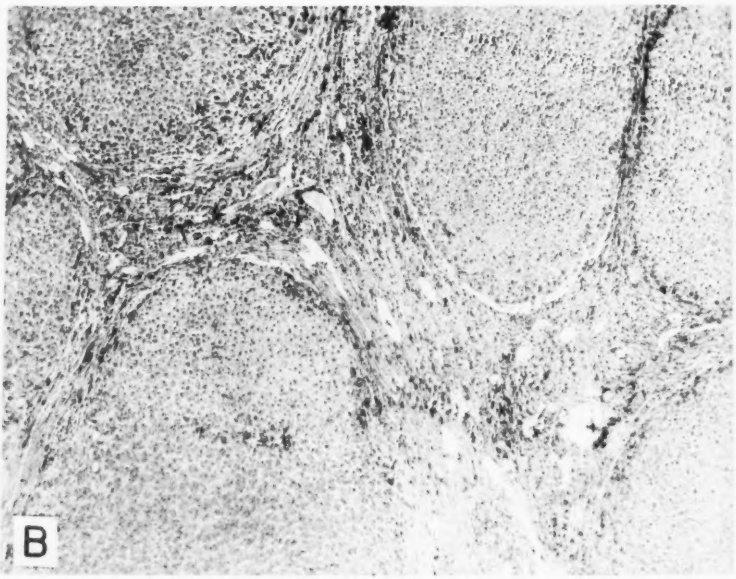


Figure 1. Liver biopsy showing large nodules with normal-appearing liver tissue, characteristic of postnecrotic cirrhosis. (A, × 14; B, × 50)

transferred to an Army hospital in the United States, where gradual improvement ensued. Her jaundice slowly subsided and the ascites drained spontaneously through the abdominal incision. Laborarory findings were essentially unchanged except for a total serum protein of only 4.3 grams per 100 ml, with a reversal of the albumin-globulin

ratio. Treatment consisted of a low-salt, adequate-protein diet, with multiple vitamins and mercurial diuretics. There was gradual clearing of the ascites and closure of the wound.

During convalescence, thrombophlebitis occurred in both legs This was managed with heparin sodium without untoward incident. After two and one-half months, the patient improved sufficiently to be discharged to her home. Since then she has been able to carry on moderate activity, and there has been no recurrence of jaundice. Minimal ascites and peripheral edema persisted for about seven months postoperatively, and then subsided. Mild infrequent pain in the left upper quadrant of her abdomen has remained. Amenorrhea also has persisted. There were no spider nevi nor any palmar erythema at any time during her illness.

DISCUSSION

In patients with juvenile cirrhosis, the clinical picture at the onset of symptoms may be confusing and difficult to diagnose. In the report of Bearn, Kunkel, and Slater, obesity, amenorrhea, fatigue, and epistaxis were all listed as presenting complaints. The patient in this report noted exertional fatigue, with epistaxis and amenorrhea as her earliest symptoms. On examination, however, only splenomegaly suggested the possibility of liver disease, until icterus appeared during her third admission.

When first seen, symptoms in these patients may suggest involvement of other systems. Amenorrhea or delayed menstruation, for instance, may suggest a primary local pathologic condition or an endocrine disturbance, particularly if associated with obesity. In the 26 patients with cirrhosis reported by Bearn and associates, all but two had hepatosplenomegaly, and these two had hepatomegaly.

In reviewing the literature on systemic lupus erythematosus, Harvey and co-workers[2] noted hepatomegaly in 35 per cent of 105 patients, and splenomegaly in 15 per cent. The liver usually extended 2 to 3 cm below the costal margin. Bromsulphalein retention tests were performed on 16 of these patients, and an abnormal retention was noted in 6. Three of these had either cirrhosis of the liver or viral hepatitis. Prothrombin times were determined in 38 patients, and in 7 showed a moderate reduction to about 50 per cent of normal. In 6 patients there was a marked reduction to less than 30 per cent activity. Vitamin K had no effect on restoration of the prothrombin time to normal. Cephalin flocculation and thymol turbidity determinations were made in 82 cases by Harvey and co-workers. They were positive in 67, probably because of altered protein relationships.

The splenomegaly in our patient, together with her very poor hepatic-function tests, should have suggested the correct diagnosis on her first admission. However, the absence of hepatomegaly and of any antecedent history of jaundice or symptoms

usually ascribed to cirrhosis, led us to a misdiagnosis. The myalgia, epistaxis, leukopenia, and hematuria noted on at least two occasions, and the repeated albuminuria, caused us to make the diagnosis of systemic lupus erythematosus. As the patient's course progressed, and after rereading the paper of Bearn and associates, it became increasingly apparent that she had liver disease and not systemic lupus erythematosus as was thought originally.

SUMMARY

Postnecrotic cirrhosis may initially resemble systemic lupus erythematosus, as illustrated by a case report of a 14-year-old girl. In young women, the prominent features of this disease are fatigue, or malaise aggravated by effort; amenorrhea, or delayed menarche; arthralgia; and jaundice. Hepatosplenomegaly, or either hepatomegaly or splenomegaly alone, may be the only significant physical abnormality encountered in the absence of jaundice.

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SPECIFICITY IN THERAPY OF THE FUTURE

"The therapy of the future will be increasingly selective and more and more will assume the sharpness of the surgeon's knife as it invades the tissue to be affected. This selectivity may in some instances lessen the threat of side reactions but in others may increase the dangers. Thus it doesn't seem practical at this time to dream of the broadly acting drug that will attack many diseases without any harmful possibilities. Antibiotics and the sulfonamides have a wide sweep in their effectiveness but they probably will not be representative of most drugs of the future. While it is possible to attach many bacteria with one agent, other health problems will require the specificity of many of the drugs now under development. While there seem to be many 'magic bullets' today in the field of chemotherapy, they cannot be expected singly to win the war against disease any more than one rifle would have taken Anzio beach in World War II."

—AUSTIN SMITH, M. D.
in *Journal of National Medical Association*
p. 294, Sept. 1957

Parkinsonism in an Oriental Treated by Chemopallidectomy

RAOUL C. PSAKI, *Lieutenant Colonel, MC, USA*
GORDON T. WANAMAKER, *Lieutenant Colonel, MC, USA*

PARKINSONISM is a disturbance of motor function, characterized chiefly by slowing and weakening of voluntary movement, muscular rigidity, and tremor. The syndrome may be produced by any of several pathologic processes. It usually is ascribed to lesions involving the corpus striatum, globus pallidus, or substantia nigra. The condition usually develops insidiously and progressively, but frequently is marked by partial remissions, plateaus, and exacerbations of varying duration. It may be unilateral or bilateral.

During the past 20 years, various surgical procedures[1-5] have been carried out to relieve the spasticity and tremor, but their success has been proportional to the sacrifice of motor power. Other technics[6] were aimed at the basal ganglia; however, high operative mortality precluded their general use. Recently, stereotactic apparatus was used by Spiegel, Wycis, and Thur[7] and Narabayashi and Okuma[8] for approach to the basal ganglia, while Fenelon and Thiebaut[9] devised methods of coagulating the ansa lenticularis and globus pallidus without the use of a stereotactic machine.

During the past several years Cooper[10-12] and co-workers devised technics aimed at the destruction of the mesial globus pallidus and its afferent connections with other basal ganglia and motor areas of the brain. The first of these was anterior choroidal artery occlusion, which aimed at infarction of the mesial globus pallidus by interfering with its blood supply. The second was chemopallidectomy,[13] which aimed at the destruction of the mesial globus pallidus by injection of absolute alcohol into this structure. It is the latter of these procedures that we have used in the case to be presented.

METHOD

The technic of chemopallidectomy described by Cooper[10] and Cooper and Poloukine[11] consists of placing a small polyethylene

Read at the Annual Meeting of the American Congress of Physical Medicine and Rehabilitation, Los Angeles, Calif., 11 September 1957.
From Tripler U. S. Army Hospital, APO 438, San Francisco, Calif.

catheter through a trephine opening in the skull into the mesial globus pallidus, under x-ray control, and injecting 0.25 ml of 1 per cent procaine. If the catheter has been correctly placed, tremor and rigidity of the contralateral extremities are almost instantaneously alleviated. Destruction of this region is then carried out by injection of 0.5 to 1 ml of absolute dehydrated alcohol.

CASE REPORT

A 43-year-old Oriental employee was admitted to this hospital on 6 January 1957 for surgical treatment of bilateral Parkinson's disease, greater on the left. His illness had been diagnosed as parkinsonism in October 1955. In retrospect, however, his original symptoms had appeared several years previously. There was no history of encephalitis. The only head trauma had occurred in 1941. At that time there was no fracture of the skull or complete loss of consciousness, even though the patient was reportedly confused for several hours. His symptoms in October 1955 involved predominantly the left arm and leg. Because of his disability he was retired from the Postal Service in May 1956.

He was first seen at this hospital in November 1956. At that time physical examination revealed masklike facies with slow speech; cogwheel rigidity of the left arm on extension, weakness of grip, and coarse tremors of the left hand which disappeared on sudden purposeful movement; rigidity of the neck muscles; awkward, shuffling gait, with the body bent forward and the left leg dragging somewhat; and minimal tremor of the right upper extremity.

Pneumoencephalographic findings on 29 November 1956 were essentially normal; there was no evidence of brain atrophy. The patient was discharged to home care, but became progressively worse during the month of December. He became unable to walk without someone supporting him, and was no longer able to bathe and clothe himself. The spasticity and tremor of the right upper extremity also increased.

On 10 January 1957, a unilateral right-sided chemopallidectomy was performed, with injection of 0.4 ml of dehydrated alcohol into the region of the globus pallidus. The patient had a rounded Oriental-type skull with almost equal anteroposterior and transverse diameters, and using the surface topography recommended by Cooper and associates[14] for the usual Caucasian-type skull, the tip of the catheter was 1 cm from the desired area (fig. 1). The radiopaque catheter accordingly was withdrawn and reinserted, using the third ventricle as a landmark, as has subsequently been recommended by Obrador.[15] The catheter had also to be inserted 0.5 cm deeper than is usual for the Caucasian-type skull (fig. 2). The catheter was allowed to remain in place, and on 14 January a second injection of 0.4 ml of alcohol was made. Postoperatively, the patient's tremor and spasticity on the left were improved but not cured. He was continued on Artane (brand of trihexyphenidyl hydrochloride) medication and given physical therapy, which consisted of exercise to

all extremities, aimed at increasing co-ordination, strength, and range of motion. The tilt table also was used to aid in balance. Occupational therapy was prescribed, primarily for the upper extremities and hands, to retrain the patient in co-ordination and bimanual activities.

Figure 1. Roentgenogram showing radiopaque catheter, the tip of which is approximately 1 cm above and lateral to the mesial globus pallidus.

The muscle test on 21 January revealed mild to moderate gross weakness, in-co-ordination with minimal tremor, and spasticity. Early in February the patient was able to ambulate with minimal assistance. On 2 April, one month after discharge, he had better control and co-ordination of his left upper extremity and was able to use his hand to soap himself in the shower. He could perform bimanual activities with greater facility.

On 28 June, examination revealed that co-ordination in sitting, balancing, standing, and walking had improved further, and there was greater ease in getting into and out of a chair. Bimanual activity was carried out with greater facility, and mental alertness and tolerance were improved.

On 12 November the patient was re-examined. There was good range of motion of all joints, with relatively good strength of all muscles. Tremor was present in both right and left hands at rest, but more marked on the right. The patient could walk unaided and carry out all his essential activities of daily living. He was discharged as considerably improved.

Figure 2. Roentgenogram showing proper position of tip of catheter in mesial globus pallidus.

SUMMARY

An Oriental patient with parkinsonism was treated with good results by chemopallidectomy followed by physical and occupational therapy. It was evident from our experience in performing the chemopallidectomy in this case, that allowance must be made for the difference in head shape in Orientals in using surface topography of the skull as landmarks. Orientation of the catheter in relation to the third ventricle seems to be the method of choice.

Physical and occupational therapy are useful adjuncts to surgical therapy in treating patients with parkinsonism.

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SORTING OF MASS CASUALTIES

"The simultaneous infliction of injuries of all degrees on a large population must be anticipated in the event of either natural or nuclear disasters. When facilities for treatment are limited, the greatest possible number of lives can be saved only by making sure that these facilities are not enhausted by injudicious use on either the trivial or the hopeless cases. Triage, the sorting of the injured, must be done by the most mature surgeon available. It decides questions of treatment, of transportation, and of return to duty. Its effectiveness is enhanced by attention to the changing tactical situation."

—H. HASKELL ZIPERMAN, Lt. Col., MC, USA
in *Journal of American Medical Association,*
p. 1438, Dec. 15, 1956

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Congestive Heart Failure of Undetermined Cause

WILLIAM R. SCHILLHAMMER, *Major, MC, USA*

CONGESTIVE heart failure usually is secondary to definite cardiovascular abnormalities, and ordinarily the origin of the syndrome can be fairly well determined. In young adults, it is a relatively rare phenomenon except in association with rheumatic or congenital heart disease, or as a complication during the course of acute glomerulonephritis, and "idiopathic" congestive heart failure is almost unknown. Rosenbaum, Nadas, and Neuhauser[1] reported several cases of what they considered to be idiopathic myocarditis in infants and children, but none in an adult.

CASE REPORT

A 29-year-old soldier was admitted to this hospital on 4 April 1957, with the chief complaint of swelling of the face and legs of two weeks' duration. The past and family histories were noncontributory. The patient stated that he had felt perfectly well until about two weeks prior to admission, when he noted the onset of painless swelling of the face. This did not trouble him at the time and he did not seek medical attention until 26 March 1957, when at his wife's insistence he reported to sick call and was diagnosed as having angioneurotic edema of the face.

It was noted by the examining physician that the patient had had two similar episodes in the past two or three years, and each time had been cutting grass prior to the onset of his difficulty. Because of this history, skin sensitivity tests were accomplished by the scratch method, but were negative. The patient was given 50 mg of Benadryl Hydrochloride (brand of diphenhydramine hydrochloride) four times daily. This did not alter his clinical status. He returned to sick call on 28 March, at which time he complained of some swelling of the abdomen. The examining physician stated that there was some edema of "the upper abdomen" and prescribed 24 mg of ephedrine sulfate four times daily in addition to the Benadryl which the patient was already taking.

Shortly thereafter the patient noted that his legs were beginning to increase in size. On 29 March he again returned to sick call because

From U. S. Army Hospital, Fort Hood, Tex.

of headaches. At that time he had typical physical findings of acute sinusitis and roentgenograms of the paranasal sinuses confirmed this diagnosis. He was treated by the application of heat to the forehead, and sodium salicylate was now added to the therapeutic regimen. The patient stated that at this time he felt that his abdomen seemed to improve but his ankle edema increased and he began to have shortness of breath on exertion. He noted that lying down on his stomach would markedly increase the shortness of breath, and found it was necessary to use two pillows rather than the usual one in order to avoid dyspnea while lying down. There had been absolutely no past history of cardiac or renal disease.

The patient returned to sick call on 4 April. At that time it was noted that his blood pressure was 180/105 mm Hg. There were rales at both lung bases, hence the patient was admitted to the hospital for further evaluation and therapy.

Physical examination on admission revealed a well-developed and well-nourished white man who was in no distress. His temperature was 98.2°F; pulse, 92; blood pressure, 170/100 mm Hg.; height, 6 feet 1 inch; weight, 160 pounds. There were numerous medium moist rales at both lung bases. The heart size was normal to percussion, and the rhythm was normal. The second aortic sound was somewhat loud, and there was a grade I systolic murmur, heard generally over the precordium. There were no diastolic murmurs. Examination of the abdomen showed the liver to be palpable two fingersbreadth below the right costal margin. It was slightly tender and smooth. No other masses were palpated. There was 2 plus pitting edema of both lower legs. The remainder of the physical examination was either negative or within normal limits.

A hemogram showed a white blood cell count of 11,400 with 73 per cent neutrophils, 2 per cent eosinophils, and 25 per cent lymphocytes. The hemoglobin was 12.5 grams per 100 ml, and the sedimentation rate was 48 mm per hour. The original urinalysis revealed a few white blood cells without other abnormal findings. The serologic test for syphilis was negative. Blood chemistry studies on 5 April showed the following values: nonprotein nitrogen, 21.6 mg per 100 ml; blood urea nitrogen, 10.2 mg per 100 ml; serum chlorides, 108 mEq/1; serum sodium, 145 mEq/1; cholesterol, 236 mg per 100 ml, with 170 mg per 100 ml as esters. The total serum protein was 5.8 grams per 100 ml (albumin, 2.9 grams, and globulin, 2.9 grams). The initial roentgenogram of the chest (fig. 1) demonstrated the heart to be the upper limit of normal size with bilateral basilar pulmonary congestion. There was a small amount of pleural fluid in the costophrenic angles bilaterally. It was the roentgenologist's opinion that these findings were typical of congestive heart failure. Fluoroscopy revealed only that the size of the heart was at the upper limit. The electrocardiogram was normal.

The patient was kept in bed and was given a low sodium diet. No other specific medications were administered. On this program he

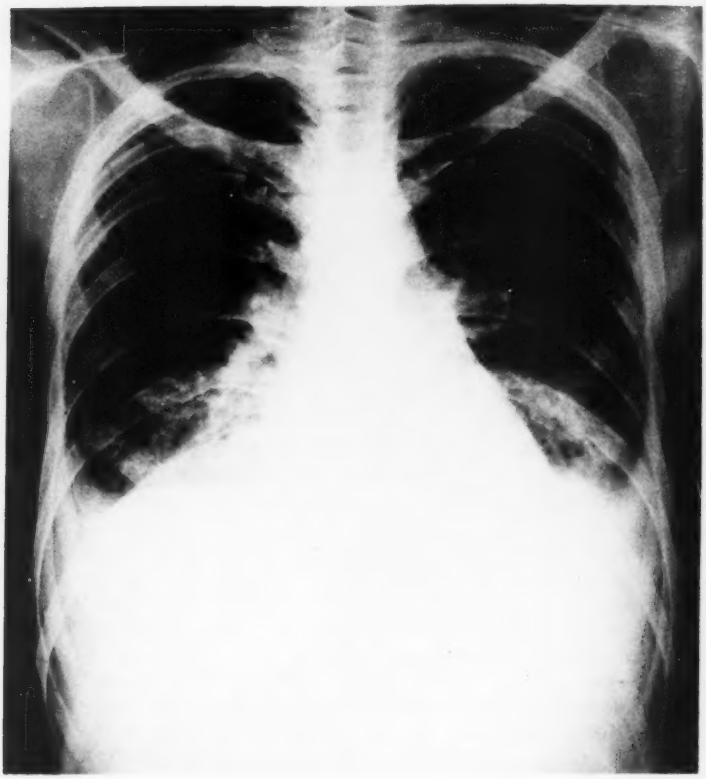

Figure 1. Roentgenogram of chest on 4 April 1957. Note increased heart size, pulmonary edema, and bilateral pleural fluid.

improved dramatically. His weight on admission was 160 pounds, and within five days he lost 18 pounds. Venous pressure on 5 April was 160 millimeters of saline. The circulation time, using Decholin (brand of dehydrocholic acid), was 14 seconds. It was thought that in this man, who was of slight stature, this time was slightly prolonged. Daily urinalyses revealed no specific abnormalities, although on 5 April there was a 1 plus albumin. After this specimen, the urine examinations were entirely normal. An Addis count was normal. A 24-hour urine sample on 8 April revealed a total protein content of 0.01 gram per liter, and repeat blood urea nitrogen and nonprotein nitrogen were normal.

On 9 April the patient was allowed to be ambulatory about the ward and was given a regular diet. The abnormal pulmonary findings cleared rapidly. The fluid in the costophrenic angles and systolic murmur heard disappeared. A roentgenogram of the chest on 10 April (fig. 2)

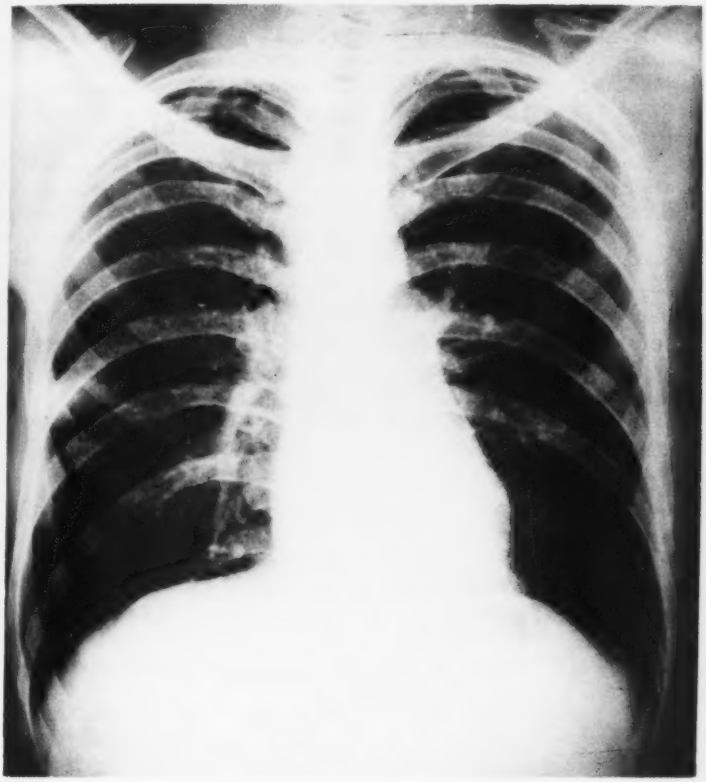

Figure 2. Roentgenogram of chest on 10 April 1957. Note decrease in heart size, and disappearance of pulmonary edema and pleural fluid

revealed decrease in the size of the heart from an original transverse diameter of 14 cm to 11 cm. Serial electrocardiograms were entirely normal.

On 18 April the patient was allowed two weeks of convalescent leave, from which he returned on 6 May, having remained entirely asymptomatic. Physical examination upon his return to the hospital revealed no abnormalities. The heart size was normal, and there were no murmurs. Blood pressure was 118/76 mm Hg.

Electrolyte studies on 6 May revealed the serum sodium to be 131 mEq/l; potassium, 4.4 mEq/l; and chlorides, 98 mEq/l. Total serum protein was 6.8 (albumin, 3.5, and globulin, 3.3) grams per 100 ml. After the initial two to three days in the hospital the patient seemed to be clinically normal. Renal function studies, urinalysis, blood urea nitrogen, and urine concentration tests, were normal at this time. An electrocardiogram and a roentgenogram of the chest were normal.

The patient was discharged to duty on 8 May and was advised to remain on limited duty for three months, after which he was returned to full military duty. He was followed as an outpatient and in serial follow-up studies it was noted that his blood pressure remained in the vicinity of 115 to 120 over 65 to 70 mm Hg. Auscultation of the heart revealed no abnormality. Electrocardiograms and roentgenograms of the chest remained normal. Basal metabolic rate was +5. The patient is at the present time (November 1957) performing full military duty and remains completely asymptomatic.

SUMMARY

This patient is presented as representing an unusual case of congestive heart failure of unknown cause. At the time of his admission to the hospital it was assumed from his clinical history that he probably had acute glomerulonephritis as the underlying cause of his difficulty. He had edema and hypertension, and an isolated urine specimen had revealed pyuria. However, serial urine studies and blood chemistry studies made this diagnosis untenable. The possibility of pericarditis was considered, but this seemed extremely unlikely in view of the normal electrocardiograms, the absence of friction rubs, and the presence of normal cardiac fluoroscopy. Hypertension in this patient was extremely short-lived and was present only during the first day of his hospitalization. There was no evidence for allergic vasculitis with myocarditis, or for acute bacterial or viral myocarditis. He recovered completely from his episode of congestive heart failure, has no residuals, and is performing full active military duty without handicap eight months after his hospitalization. It is most unusual for a 29-year-old, healthy, white man to develop acute congestive heart failure, and yet this is the case in this individual. He recovered quickly with bed rest and a low sodium diet. It is thought that the latter had nothing to do with the patient's recovery, however. Digitalis was not used in the management of this case.

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AERO MEDICAL ASSOCIATION MEETING

Geared to the forthcoming age of space travel, more than 100 speakers will present the latest research and development achievements in the biologic aspects of flight at the 29th annual meeting of the Aero Medical Association at the Statler Hotel, Washington, D. C., 24, 25, and 26 March 1958. Captain Ashton Graybiel, MC, USN, director of research at the U. S. Naval School of Aviation Medicine, is president of the society.

Sessions on space flight will be held on the afternoons of 24 and 26 March under the chairmanship of Colonel Paul A. Campbell, USAF (MC), and Doctor Hubertus Strughold, respectively. The program also includes papers on acceleration, oxygen equipment, hypoxia and hyperoxia, human behavior, sensory problems, hyper- and hypothermic stress, physiology, psychology, civil aviation medicine, and clinical problems.

Captain Graybiel

The fourth Louis H. Bauer lecture, established in 1955 as a tribute to the Association's founder and first president, will be presented on 24 March as a part of the opening ceremony of the meeting, by Doctor Rodolfo Margaria, distinguished professor of physiology and biochemistry at the University of Milan. He will present new phases of recent work in acceleration and fatigue.

In addition to a full scientific program, Captain Graybiel will be host at an international reception for visiting members and guests from other countries at the Officers' Mess of the National Naval Medical Center, Bethesda, Md., on the evening of 25 March. He will also preside at the traditional banquet of the Association at the Statler Hotel on 26 March when the recipients of the Association's four awards for aeromedical achievement will be announced.

Brigadier General M. S. White, USAF (MC), president-elect of the Aero Medical Association, will be installed as Captain Graybiel's successor. The Airline Medical Directors' Association and the Civil Aviation Medicine Association will hold concurrent meetings in Washington.

A MESSAGE FROM THE A. M. A.

Two resolutions introduced during the 3 to 6 December 1957 meeting of the American Medical Association in Philadelphia are of particular interest to physicians in the military services. One of these concerns service membership in the Association and the other recommends a program to encourage participation of federal service physicians in local medical societies.

Resolution No. 7 was referred to the Reference Committee on Amendments to the Constitution and Bylaws. In view of the complexity of this question, which involves changes in the constitution and bylaws of the Association, the Committee recommended that the matter be referred to the Council on Constitution and Bylaws for further study. The recommendation was adopted by the House of Delegates, and provides as follows:

Whereas, A basic principle of organized medicine in America holds that an applicant's qualifications for membership should be evaluated by his local colleagues and that, when he is elected to membership in a county medical society he should then, and then only, become a member of his state medical association and the American Medical Association; and

Whereas, Direct Service Membership in the American Medical Association designed to meet certain necessities of career officers in the Armed Forces of the United States, has over the years been expanded far beyond that original concept and has reached the point where it now includes most of the physicians employed by the federal government and removes them from any responsibility to their county and state medical organizations, thus violating the basic principle referred to above; and

Whereas, This expansion has come about largely through piece-meal amendment of the Constitution and Bylaws of our Association, some sections of which appear to conflict with each other in matters of choice between dues-exempt Active Membership and direct Service Membership; and

Whereas, Conflicts or optional choices between such membership sections of the Constitution and Bylaws have recently been interpreted by the Board of Trustees and the General Officers in favor of further expansion of Service Membership; now therefore be it

Resolved, That the House of Delegates reiterates its adherence to the principle that membership in this Association should originate with membership in a component county medical society, and instructs the Council on Constitution and Bylaws to prepare the necessary

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From the Council on National Defense of the American Medical Association. The views and opinions expressed are not necessarily those of the Department of Defense. —*Editor*

amendments to return Service Membership to the original concept of its applicability only to the career officers of the Armed Forces of the United States; and be it further

Resolved, That pending implementation of these amendments, the Board of Trustees and the General Officers are instructed to resolve existing conflicts within the Constitution and Bylaws related to this subject matter in favor of dues-exempt active membership through component societies and constituent associations rather than in favor of direct Service Membership.

Resolution No. 29 was referred to the Reference Committee on Medical Military Affairs. The reference committee recommended adoption of the resolution with minor changes in its language. This was adopted by the House of Delegates. As approved, the resolution provides as follows:

Whereas, There are approximately 10 per cent of the active, practicing membership of the A. M. A. in Federal Medical Services, increasing annually the relative percentage of these physicians to the total number of practicing physicians; and

Whereas, These physicians are not dues-paying members of the A. M. A., nor may they vote; and

Whereas, Active participation of these physicians is sorely needed in all county and state medical association; and

Whereas, In most if not all county medical societies there are relatively few members of the Federal Medical Services participating to any extent in the activities of these local medical societies; and

Whereas, It is extremely difficult to enlist active participation of these physicians in local medical societies especially if dues, however small, are charged as long as non-paying membership in the A. M. A. is offered, and therefore be it

Resolved, Membership in the American Medical Association of physicians engaged in Federal Medical Services be reconsidered by the Council on Constitution and Bylaws; that this council be requested to seek means of increasing active participation of physicians in this classification and in local medical societies; and be it further

Resolved, That the Council on National Defense, through its Committee on Military Medical Affairs, assist in the accomplishment of this objective and report back to the House of Delegates of the A. M. A. in 1958; and be it further

Resolved, That the Surgeons General of the Army, Navy, Air Force and Public Health Service, Veterans Administration and other allied branches be requested to participate in this program and that special recognition or credit be granted to physicians in Federal Medical Services who participate actively in local medical societies.

DEATHS

BURNS, John Albert, Captain, USAFR (MC), of Atlanta, Ga.; stationed at the 3906th U. S. Air Force Hospital, APO 117, New York, N. Y.; graduated in 1953 from the Medical College of Georgia, Augusta, Ga.; commissioned a First Lieutenant in the United States Air Force Reserve 4 August 1955; ordered to active duty 6 May 1956; died 19 January 1958, age 28, near Port Lyautey, French Morocco, as the result of an aircraft accident.

CALKUM, John Foley, Captain, USAFR (MC), of Denver, Colo.; stationed at the 3882d School Group, Gunter Air Force Base, Ala.; graduated in 1955 from the University of Colorado School of Medicine, Denver, Colo.; commissioned a First Lieutenant in the United States Air Force Reserve 23 June 1955; ordered to active duty 1 July 1955; died 19 December 1957, age 29, near Benton, Ala., as the result of an aircraft accident.

HARRADINE, Frank Frederick, Captain, USAFR (MC), of Santa Maria, Calif.; stationed at the 22d Tactical Hospital, March Air Force Base, Calif.; graduated in 1955 from the University of California School of Medicine, Berkeley-San Francisco, Calif.; commissioned a Captain in the United States Air Force Reserve and ordered to active duty 8 September 1956; died 18 December 1957, age 27, near Mount Palomar, San Diego County, Calif., as the result of an aircraft accident.

JOHNSON, Ivar Carl, Lieutenant Colonel, DC, AUS, of Benton Harbor, Mich.; stationed at the 123d Medical Detachment, 188th General Dispensary, Germany; graduated in 1931 from the University of Michigan School of Dentistry, Ann Arbor, Mich.; commissioned a Lieutenant Colonel in the United States Army Reserve 28 September 1953; ordered to active duty 8 February 1954; died 11 December 1957, age 51, in Germany, of myocardial infarction.

STOLTZ, Ray Elmer, Colonel, MSC, USA, of Indianapolis, Ind.; stationed at Fort Sam Houston, Tex.; commissioned a Captain in the Army of the United States and ordered to active duty 16 September 1942; commissioned a Major in the United States Army 5 July 1946; died 20 December 1957, age 51, at Brooke Army Hospital, Fort Sam Houston, Tex., of a cerebrovascular accident.

YATES, Marion Twitty, Captain, MC, USN, of Darlington, S. C.; stationed at U. S. Marine Corps Air Station, Miami, Fla.; graduated in 1935 from the Medical College of South Carolina, Charleston, S. C.; appointed a Lieutenant, junior grade, in the United States Navy 1937; died 14 December 1957, age 48, at the U. S. Marine Corps Air Station, Miami, Fla., of coronary thrombosis.

EDITORIAL

THE MULTIPLICITY OF CERTAIN UPPER GASTROINTESTINAL LESIONS

Two special features of the diseases of the upper gastrointestinal tract contribute uniquely to the difficulty of clinical diagnosis. Perhaps the source of greatest confusion is the propensity of localized lesions to produce important nearby and far-removed visceral dyskinesias which, more than the lesion itself, become responsible for symptoms. Thus, many of the diseases produce similar complaints.

Second, more than any other organ system, the gastrointestinal tract is peculiarly susceptible to synchronous multiplicity of localized lesions. In some cases, such as Saint's triad (hiatus hernia, gallstones, and diverticulosis of the colon), combinations occur with such regularity that some causal association must be assumed. In others, the associations seem haphazard. The possible specificity of such associations is of considerable practical and theoretical importance, but for the present study the question was simply one of how frequently the clinician might expect to encounter another nearby lesion in the upper gastrointestinal tract after one has been detected.

To obtain an impression from personal experience, the lesions shown in table 1 were selected, and charts were reviewed until data from the numbers indicated had been collected. The lesions were chosen with several criteria in mind: they are lesions of the gastrointestinal tract proper; they occur in rather close anatomic relationship

TABLE 1. *Lesions associated with various lesions of the upper gastrointestinal tract*

	Number of cases	Per cent with								
		Another lesion	Esophageal ulcer	Esophageal diverticulum	Esophageal carcinoma	Hiatus hernia	Gastric ulcer	Gastric diverticulum	Gastric carcinoma	Duodenal ulcer
Esophageal ulcer	30	40	-	6.7	3.3	20	3.3	-	3.3	13
Esophageal diverticulum	35	46	5.7	-	2.9	23	2.9	-	2.9	12
Esophageal carcinoma	30	6.7	-	3.3	-	-	3.3	-	-	-
Hiatus hernia	250	25	2.4	3.2	-	-	11	1.2	0.8	14
Gastric ulcer	250	32	0.4	0.4	0.4	11	-	0.4	0.4	25
Gastric diverticulum	20	30	-	-	-	15	5.0	-	-	20
Gastric carcinoma	100	7.0	-	1.0	-	2.0	1.0	-	-	7.0
Duodenal ulcer	1000	10	0.4	0.4	-	3.6	6.2	0.4	0.7	-

to one another; they represent benign, malignant, and mechanical lesions; and, although the patients in each category were consecutive clinic and ward patients, investigated only as the individual clinical situations warranted, they necessarily had approximately the same diagnostic studies (upper gastrointestinal roentgenography in all, esophagogastroscopy in most, and examination at operation or autopsy in many).

The findings shown in the table need little explanation or comment. Obviously, when a sick person is found to have two distinct lesions in the organ system which is responsible for the symptoms, the chances are good that one of the lesions either has caused no illness, being detected merely by a fortuitous examination, or has some etiologic relationship to the other lesion. The first explanation seems especially likely for many of the cases of esophageal diverticulum, and the second for cases of multiple lesions associated with hiatus hernia. Patients with carcinoma were found least likely to have an associated lesion. Those with duodenal ulcer were surprisingly free of second lesions, unlike the situation found in the cases of gastric ulcer. Conversely, when some other lesion was present, duodenal ulcer was a very common accompanying problem.

EDDY D. PALMER, *Lieutenant Colonel, MC, USA*
2d General Hospital
APO 180, New York, N. Y.

World Congress of Gastroenterology To Be Held in Washington, D. C.

The First World Congress of Gastroenterology (Host Organization: American Gastroenterological Association) will be held in the United States, in Washington, D. C., from 25 to 31 May 1958 at the Sheraton-Park Hotel.

Over 200 national and international scientists, physicians, surgeons, roentgenologists, and parasitologists will present the most recent clinical and investigative advances in gastroenterology. Those scheduled to appear on the program will include 36 from the United States and over 160 from 43 other countries. Simultaneous interpretation of the papers presented will be in four languages, including German, Spanish, French, and English.

For information relative to the World Congress of Gastroenterology, attendance, accommodations, registration, program, activites, et cetera, contact Dr. H. Marvin Pollard, Secretary General, World Congress of Gastroenterology, University Hospital, Ann Arbor, Mich.

ARMY NURSE RECEIVES BOVARD AWARD

Captain Lenora B. Weirick, ANC, Letterman Army Hospital, San Francisco, California, was selected to be the first recipient of the Evangeline P. Bovard Award.

This award was established in honor of Evangeline P. Bovard, an Army nurse from 1912 to 1916 and from 1916 to 1917, with an outstanding record of service in various assignments. Following her death at Letterman Army Hospital in 1955, her husband, Colonel Robert Skelton, MC, USA, Retired, set up this commemorative award by creating an endowment trust fund of assets totaling approximately $25,000, the earnings of which are to be presented annually "for the use and benefit of Army nurses assigned to Letterman Army Hospital."

Captain Weirick

Standards for the selection of the individual nurses are based principally on the Florence Nightingale Pledge for Nurses. . .

> *"I will do all in my power to maintain and elevate the standards of my profession. . . With loyalty will I endeavor to aid the physician in his work; and, devote myself to the welfare of those committed to my care."*

Captain Weirick was selected because of her outstanding qualities in the care of acutely ill patients, her invaluable contributions to improve the care of paraplegics, and her ability to instruct and train corpsmen that they might become proficient in the care of neurosurgical patients. She is a member of the Regular Army, and received the Bronze Star for meritorious service in Korea with a Mobile Army Surgical Hospital from 6 April 1951 to 22 April 1952.

The Evangeline P. Bovard Award, consisting of a citation, certificate and check, was presented to Captain Weirick by Brigadier General Paul S. Fancher, commanding general of Letterman Army Hospital, in a ceremony at the hospital on 14 January 1958.

WALTER REED RESEARCHER RECEIVES PATENT FOR COSMETIC GLOVE

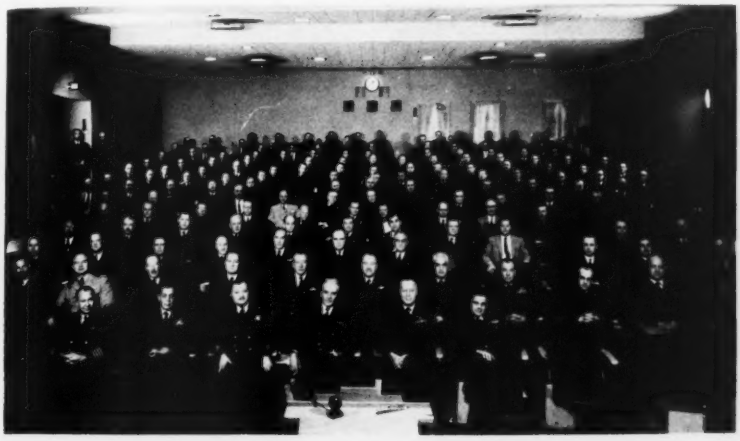
A Letters Patent for an improved prosthetic hand covering that defies detection even on close inspection was presented on 7 January 1958 to the coinventor, Carl A. Nielson of the Army Prosthetics Research Laboratory, Walter Reed Army Medical Center, by Major General Leonard D. Heaton, Commanding General of the Center.

From left to right: Mr. Carl A. Nielson, holding Letters Patent; Major General Leonard D. Heaton, Commanding General of Walter Reed Army Medical Center; and Colonel Maurice Fletcher, Director of the Army Prosthetics Research Laboratory.

Working together, Mr. Nielson and Mr. Clare L. Milton, Jr., of Baltimore, developed a process for the manufacture of a "cosmetic glove" which can be fitted over a prosthetic hand provided for amputees, or can cover hand injuries that leave disfiguring scars. The glove can be made to match the wearer's own hand in color and skin texture, and all lines, markings, and contours of a normal hand can be duplicated. In addition, natural hairs or nylon threads can be added to the glove to increase its natural appearance. The glove is made by pouring plastic into a negative mold of a model hand. Pigmentation is then added to conform to the hand to be matched.

The inventors have assigned rights to the Government of the United States to manufacture and use their process for governmental purposes without payment to them of any royalty.

ARMED FORCES MEDICAL SYMPOSIUM



Doctor Edward H. Cushing, Deputy Assistant Secretary of Defense (Health and Medical), headed a group of more than 200 senior military medical officers and civilian physicians, show above, who attended the Armed Forces Medical Symposium at Sandia Base, New Mexico, from 6 to 10 January 1958. The medical symposium was especially designed to orient medical service officers of the Armed Forces concerning special medical problems and the most current special weapons information. In addition, the latest developments in the application of atomic energy and a discussion of the related medical problems in the field of nuclear research was presented. The program was arranged under the direction of Colonel Lawrence B. Hanson, MC, USA, Staff Surgeon of the Armed Forces Special Weapons Project. It is planned that similar courses will be held in the future in order that the most recent developments on the biological and medical aspects of the atomic age may be disseminated widely throughout our armed services.

Reviews of Recent Books

MEDICAL DEPARTMENT, UNITED STATES ARMY, Surgery in World War II. Orthopedic Surgery in the Mediterranean Theater of Operations, by *Oscar P. Hampton, Jr.,* M. D., F. A. C. S., Col., MC, USAR. 368 pages; illustrated. Editor-in-Chief, Colonel *John Boyd Coates, Jr.,* MC; Editor for Orthopedic Surgery, *Mather Cleveland,* M. D.; Associate Editor, *Elizabeth M. McFetridge,* M. A. Historical Unit, Army Medical Service, Office of the Surgeon General, Department of the Army, Washington 25, D. C., 1957. For sale by the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C. Price $4.

This volume is a record of tribulations encountered in the care of wounds involving bones and joints in the early days of the fighting in North Africa and of the surgical principles and technics that were eventually evolved. Much of this knowledge that was gained by trial and careful evaluation of the results had been evolved on a limited scale in the closing phases of World War I and then forgotten. This book and the companion volumes from the other theaters are our best insurance that these sound principles and technics will be available right from the beginning of any future hostilities.

The section on initial surgery of compound fractures is especially rewarding. It describes the treatment from first aid and resuscitation through the actual technic of wound excision or "débridement" in a manner that should be understandable to the inexperienced who will use this manual as a guide. It describes the reparative phase of surgery, the object of which is to convert an open wound to a closed one within 10 days of the initial débridement. Other sections deal in a similar fashion with wounds of joints and with amputations.

About half of the book is devoted to the management of regional problems such as fractures of the humerus, both bones of the forearm and wounds of joints, and the description of the technics that were evolved for their management. This is the best manual detailing the management of skeletal wounds that I have seen. The illustrations are numerous, well chosen, and well reproduced. This book should be on the shelves of all surgeons.—*WILLIAM S. STRYKER, Capt., MC, USN*

PRINCIPLES OF SURGICAL PHYSIOLOGY, by *Harry A. Davis,* M. D., C. M., F. A. C. S. Foreword by *Lester R. Dragstedt,* M. D., F. A. C. S. 841 pages; illustrated. Paul B. Hoeber, Inc., Medical Book Dept. of Harper & Bros., New York, N. Y., 1957. Price $20.

This complete work constitutes a compilation of the physiologic concepts in a surgical frame of reference. In no other book have I been able to find such a broad and yet detailed treatment of the various concepts of surgical physiology and biochemical facts. The contents are arranged in two parts, "General Principles" and "Systemic Physiology." It has an excellent and complete index and a useful appendix of values and formulas which enhance the value of this book as a quick reference for the busy surgeon.

Part I includes all the general physiologic problems. The presentation on water electrolytes and acid-base balance tends to be tedious as is the case with almost all such detailed and technical information. The mastery of this section is extremely important in the proper treatment of radical exenterations, enterocolitis, and fistulae. If one feels an acute lack of information regarding physiologic anesthesia, he will find here a clear and precise discussion of the surgeon's responsibilities. The effects of operative trauma are clear and pertinent. Many conditions requiring surgery are analyzed in regard to the advantages and disadvantages of the accepted positions on the operating table.

Part II is, in brief, a review of the systemic physiology. Each chapter is short yet surprisingly comprehensive in the description of pathologic states and their inherent physiologic derangements. The treatment of the circulatory dynamics in the various congenital cardiac lesions, including catheterization data and clinical findings, is as lucid as I have ever seen. Liver function tests, differential diagnosis of jaundice, and various surgical problems, including partial hepatectomy and shunting procedures, are meticulously described in the chapter on liver and bile ducts. The treatment of hepatic insufficiency omits the use of glutamate, preparatory enemas, potassium salts, and 10 per cent carbon dioxide. The urinary tract is amply discussed with commendable portions on the process of micturition and the genesis of nephrolithiasis. The nervous system section is well balanced, and the discussion and the diagrams of neuroanatomy and the effects of the various lesions are good in that the most esoteric landmarks are omitted.

This book is recommended as a guide for all surgeons and would be especially useful in residency training programs. It should also be included in the library of the physician in other fields who thinks physiologically and appreciates this necessity in his practice.

—*RAYMOND A. LAWN, Col., USAF (MC)*

J. A. M. A. CLINICAL ABSTRACTS OF DIAGNOSIS AND TREATMENT, Published with the Approval of the Board of Trustees, *American Medical Association.* 564 pages. Intercontinental Medical Book Corp. with Grune & Stratton, Inc., New York, N. Y., 1957. Price $5.50.

The editor of this volume has presented the medical profession with a collection of abstracts selected from those published during the year 1956 in the abstracts section of the *Journal of the American Medical Association.* He states in the preface that he selected those abstracts which he considered "to pertain most directly to the two most important aspects of clinical medicine—diagnosis and treatment." The large quantity of current world literature makes abstracting services useful and important. Additional culling of abstracts already published in a widely read journal is a somewhat different approach to the problem. The service in the *J. A. M. A.* is good and widely disseminated; several journals have very fine abstracting services,

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and excellent independent services are available, all of which give amazingly rapid abstracting service. The particular criteria of selection mentioned by the editor and organization of the material according to anatomic systems, which is used in this collection, will no doubt appeal to some, although this will depend on the philosophy of the individual physician. The book is modestly bound and the format resembles that used in the abstracts section of the *J. A. M. A.* The index is adequate. —*JOHN K. SPITZNAGEL, M. D.*

ESSENTIALS OF CLINICAL PROCTOLOGY, by *Manuel G. Spiesman,* M. D., B. S., L. L. D., F. I. C. P., and *Louis Malow,* M. D., B. S., F. A. C. S. 3d edition. Grune & Stratton, Inc., New York, N. Y., 1957. Price $8.75.

As the title implies, this is a short, concise review of the more common diseases and deformities of the anorectal region. One chapter, devoted to "Coccygodynia and Proctalgia Fugax," calls attention to a condition frequently overlooked. The book compares favorably with others of its kind by different authors. It could readily be recommended for senior medical students, interns, and the practitioner who performs proper proctologic examinations, with occasional surgery.

—*GEORGE M. LYNCH, Capt., MC, USN*

NEW RESEARCH TECHNIQUES OF NEUROANATOMY, A Symposium Sponsored by the National Multiple Sclerosis Society, edited by *William F. Windle,* Ph. D., Sc. D. Foreword by *Frederick L. Stone,* Ph. D. 98 pages; illustrated. Charles C Thomas, Publisher, Springfield, Ill., 1957. Price $4.75.

The technics discussed in this symposium include tissue culture, electron microscopy, silver impregnation of degenerating axons, silver staining of synaptic terminations, radioautographs for measuring blood flow in various areas, quantitative histochemistry and histochemical localization of cholinesterases. From the usual approach of devising different staining technics, a new method emphasizes synaptic endings while another provides for better determination of fiber terminations, as well as for comparison with sections stained by other procedures. From the younger art of tissue culture it appears as though normal activity of both neuron and sheath cell are necessary for myelin formation. It also appears as though the action of serotonin or lysergic acid diethylamide (LSD) has an appreciable effect on the pulsatile function of oligodendrocytes. Electron microscopy discloses detailed structures within cells plus the structural relationship of cells to each other.

A more deviant device called radioautography reveals blood flow in gray matter to be faster than in white matter and further reveals different functional areas of cat cortex to have different rates of blood flow. Toward the latter part of the symposium, there are presentations which deal with histochemical technics. Through substrates and inhibitors, data concerning localization and function of the cholinesterases is obtained. Microscopic quantitative histochemistry may

open even greater vistas. Knowledge obtained from implementation of these technics is presented in a clear and concise manner so that either the devotee or neophyte may readily learn about recent advances in the field of neuroanatomic research. The bibliography enhances acquisition of this information. —*ARTHUR J. LEVENS, Lt. Col, MC, USA*

HYPOPHYSECTOMY, edited by *O. H. Pearson,* M. D., F. A. C. P. American Lecture Series, Publication No. 315, A Monograph in The Bannerstone Division of American Lectures on Tumors, edited by *David A. Karnofsky,* M. D. 154 pages. Charles C Thomas, Publisher, Springfield, Ill., 1957. Price $5.

Those interested in obtaining information concerning the relatively new procedure of hypophysectomy will find in this monograph a comprehensive appraisal of the status of hypophysectomy by surgical and radiological methods. The results of treatment of patients with cancer of the breast, other types of malignancies, and with vascular complications of diabetes mellitus by hypophysectomy are detailed by investigators who have become recognized authorities in this field. The physiologic effects of removal of the pituitary gland are presented. Details of management of the hypophysectomized patient during and after surgery are given.

An interesting feature of this monograph is the presentation, at the end of each of the four chapters, of the questions, answers, and comments that arose during discussions by the participants to the conference from which the material for this monograph originated. It should be read by everyone concerned with the management of patients who have cancer of the breast.—*GEORGE F. PEER, Col., MC, USA*

METHODS OF GROUP PSYCHOTHERAPY, by *Raymond J. Corsini,* Ph. D. 251 pages; illustrated. The Blakiston Div., McGraw-Hill Book Co., Inc., New York, N. Y., 1957. Price $6.50.

This book is a comprehensive review of group psychotherapy, apparently the first of its kind, directed to practitioners and students of the "helping professions," psychiatrists, psychologists, social workers, teachers, guidance workers, and others who deal with groups in therapeutic settings. The author includes the history, the various theories and the practice of group psychotherapy in its several manifestations. He ardently subscribes to group therapy as a useful and necessary process, and emphasizes the importance of the therapist, but seems puzzled by the question of who should be a therapist and how such a person should be trained. The stress on the socioeconomic origin of neuroses in his thinking is exemplified by the following "philosophical viewpoint:" "The writer is against psychotherapy. He wished that it did not have to exist. How much better life would be if everyone practiced mental hygiene and were so treated that no one would have those problems we call neurotic!" This completely negates or ignores the biologic drives as a factor in neurotic illness. The second part of the volume gives sample records of the several

types of group psychotherapy he calls analytic, nondirective, psychodramatic group psychotherapy and family counseling.

There is an extensive bibliography, a directory of visual aids available in this field for teaching, and good author and subject indexes. The book is clearly written and gives evidence of the tremendous work involved in preparing such an encyclopedic volume. It merits reading by anyone involved in the "helping professions."

—FELIX H. OCKO, Capt., MC, USN

PERIPHERAL CIRCULATION IN HEALTH AND DISEASE, by *Walter Redisch*, M. D., F. A. C. P., and *Francisco F. Tangco*, M. D., B. S., with a special section by *R. L. deC. H. Saunders*, M. D., F. R. S. E., and associates. 154 pages; illustrated. Grune & Stratton, Inc., New York, N. Y., 1957. Price $7.75.

This small book is limited to the diagnostic and therapeutic approaches to the problems of the peripheral vascular system. Chapters on anatomy and physiology are included. Illustrations of the vascular anatomy would be much more effective than word description alone. Vascular derangements are classified into three main categories: acute intrinsic vascular disorders, chronic intrinsic vascular disorders, and vascular disorders from extrinsic causes. This appears to be a practical approach. The chapters on collateral circulation and venous impairment are very well written. The volume represents a concise integrated approach to peripheral vascular disorders and helps to clarify thinking in this field. The rather extensive bibliography offers guides for more extensive reading on the subject. *—JOHN B. MacGREGOR, Capt., MC, USN*

THE HUMAN BRAIN, From Primitive to Modern, by *A. M. Lassek*, M. D., Ph. D. 242 pages. Charles C Thomas, Publisher, Springfield, Ill., 1957. Price $4.75.

This book touches on an extremely wide range of subjects relating to the human brain, including its developmental, morphologic, psychologic, and sociologic aspects. Necessarily brief and relatively superficial, discussions are included on a host of subjects relating to the brain, such as historical speculation on the orgin of man, brain anatomy and localization of cerebral functions; the psychological aspects of magic, religion, and tribal behavior; the sociologic and political problems arising as man and civilization develop; and thumbnail descriptions of ancient and medieval civilizations, including explorations into Greek mythology. The major theme of the book, written in simple and essentially nontechnical language, is the development of the mind and emotions, a functional, psychologic, and philosophic treatment rather than a morphologic one. Its broad coverage results in a relatively brief and superficial discussion of the many facets mentioned above. The book is well written for broad and general orientation on the human brain. It contributes relatively little to those already professionally oriented in the various aspects treated, but constitutes an interesting, broad coverage for those in unrelated fields.

—NELSON S. IREY, Lt. Col., MC, USA

THE PRINCIPLES OF THERAPEUTICS, by *J. Harold Burn,* M. A., M. D., F. R. S. 278 pagés; illustrated. Charles C Thomas, Publisher, Springfield, Ill., 1957. Price $5.50.

This volume contains a series of lectures given to his students by the author, who is professor of pharmacology at the University of Oxford. He succeeds admirably in linking pharmacology to therapeutics. The first few chapters contain a review of some primary physiologic principles and, in this section, there is well-written chapter concerning the properties of acetylcholine. The remainder of the book is concerned with a basic review of the properties of some of the more useful of the pharmacologic agents. In these chapters are included discussions of digitalis, barbiturates, endocrine glands and their pharmacologic relations, and antibiotics. Each subject is well covered in a brief manner, and could be recommended for use either by a medical student or by the practicing physician. As is inevitable in a book of this type, in view of the rapid advances in the field, the antibiotics seem to be sketchily covered from the standpoint of today's medicine. The volume is attractively bound and has an excellent index. A few pertinent references are listed at the end of each chapter. This book may serve for review purposes for the medical student, or for the practicing physician who desires a brief discussion of the subject of pharmacology and its relation to therapeutics at a rather basic level.

—*JOHN E. GORMAN, Capt., MC, USN*

THE CLINICAL ASPECTS OF ARTERIOSCLEROSIS, by *Seymour H. Rinzler,* M. D., F. A. C. P. 339 pages; illustrated. Charles C Thomas, Publisher, Springfield, Ill., 1957. Price $8.75.

The purpose of this volume is to assemble uner one cover the necessary information needed for a practicing physician to understand, diagnose, and treat the degenerating disease state of arteriosclerosis. The first chapter on general considerations attempts to clarify basic investigations of a morphologic, physiologic, biochemical, geopathologic, and epidemiologic nature. The author stresses the accepted generalized nature of this disease, and then tends to take sides on the highly controversial dietary vagaries which can be slanted in either direction by the authors quoted. This problem may or may not be urgent; however, I, for one, feel that individual emotions and the scientific competition among investigators should not be allowed to affect our thinking on this matter.

The cardiac aspects of arteriosclerosis is included in a chapter devoted to the anatomy and diagnosis (including tests designed to elucidate latent disease) of the coronary arteries. The following chapter on differential diagnosis of chest pain is rather brief and does not elaborate on the truly clinical evaluation of sectional pain.

The chapter on treatment of effort angina contains only medical therapeutic agents and covers briefly the usual drugs and a wide variety of questionable ones such as vitamin E, cytochrome C, x-radiation

of the adrenals, cobra venom, et cetera. Another on surgical therapy is detailed only insofar as the author's technic of injecting or using ethyl chloride spray on trigger zones is concerned. Congestive heart failure is taken up from a therapeutic viewpoint but such topics as the toxicity of digitalis and the use of potassium salts are incomplete. Disorders of the heart beat are similarly discussed. The cerebral aspects of arteriosclerosis are presented in an excellent chapter with an especially fine chart on the syndrome of the brain stem modified from Jelleffe and White by Dr. Brock. The peripheral vascular aspects are equally well done although relatively brief in content.

This volume is concluded with short chapters on the retinal, renal, and pulmonary manifestations of this condition. The following typographic errors were noted: page 193, the page title refers to a previous chapter; page 91, medial dissection is spelled "medical"; and on page 101, coronary is spelled "cooronary." Although this book may be quite useful to a general practitioner or the intern, I doubt that it is detailed or complete enough to be of value to the specialist.

—LESTER J. POPE, Capt., MC, USN

THE YEAR BOOK OF CANCER (1956-57 Year Book Series). Compiled and edited by *Randolph Lee Clark, Jr.,* B. S., M. D., M. Sc. (Surgery), D. Sc. (Hon.), and *Russell W. Cumley,* B. A., M. A. Ph. D. 572 pages; illustrated. The Year Book Publishers, Inc., Chicago, Ill., 1957. Price $7.50.

This is a newcomer in the series of Medical Year Books. Its need has become increasingly apparent because cancer has become more and more the responsibility of every member of the medical profession. Those in the medical profession actively engaged in the care of the cancer patient cannot always devote sufficient time to the literature in keeping abreast of the advance in oncologic knowledge so necessary in the intelligent handling of patients afflicted by malignancy. This volume provides comprehensive abstracts of significant articles in the field of oncology which have appeared during the preceding year. For the most part the articles abstracted relate to clinical cancer, although some discuss results of basic research.

In compiling this book a consulting editorial board of 119 members was established, which reflected the ultimate in authority on all aspects of cancer and the broadest possible intimacy with the world literature. The field of oncology was then divided into 25 sections and to each section was assigned a number of the editors. It was these groups who selected the 207 articles to be abstracted. The editors have done well in condensing a large volume of material into this book. Editorial comments throughout the book are sagacious and pointed in nature. Although it is not a substitute for medical literature, these abstracts will permit the reader to keep up-to-date in the broad field of oncology. It should be of great value to physicians in general, but particularly so to those treating cancer. *—HAROLD G. YOUNG, Capt., MC, USN*

MODERN PERINATAL CARE, by *Leslie V. Dill,* M. D., F. A. C. S. 309 pages; illustrated. Appleton-Century-Crofts, Inc., New York, N. Y., 1957. Price $6.50.

The author of this book, an outstanding obstetrician and teacher, succeeds in presenting the important subject of perinatal care in a concise practical manner. This permits the reader to evaluate his own ideas and practices for the purpose of perhaps discarding certain outmoded useless procedures and treatments, and substituting, accepting, or re-emphasizing the importance of certain others. Graphic figures, which at a glance permit the reader to grasp and retain the subject material under discussion, are used generously. Because these are not of exact statistical detail, they are all the more valuable in focusing attention toward frequency rates of the more important obstetric conditions. Similarly, treatments are presented in table form, in addition to the normal discussion, so that the physician may easily retain the salient features in therapy for immediate use in the hospital, office, or patient's home.

The chapter on fetal and neonatal mortality is a definite contribution to this frequently discussed subject for it points out the way along which we must travel to further reduce the incidence of stillbirths and neonatal deaths. The two concluding chapters on medicolegal and religious problems encountered in obstetrics are particularly praiseworthy. In the former, the author skillfully touches on each important legal pitfall in everyday practice so that the physician may recognize them and be duly warned. In the last chapter the author tactfully presents Catholic ethics and does so in a manner to help overcome misunderstanding on the part of the layman and physician.

This book will find ready acceptance in the personal library of the obstetrician as well as in the hospital library. Its clarity and readability coupled with its conservatism will ensure its popularity with students.

—*MORRIS M. RUBIN, Capt., MC, USN*

Craig and Faust's CLINICAL PARASITOLOGY, by *Ernest Carroll Faust,* A. B., M. A., Ph., D. and *Paul Farr Russell,* M. D., M. P. H., with the Editorial Assistance of *David Richard Lincicome,* B. S., M. S., Ph. D. 6th edition. 1,078 pages; 346 illustrations; 7 plates in color; 23 tables. Lea & Febiger, Philadelphia, Pa., 1957. Price $15.

The sixth edition, of this highly successful and widely used text and reference book has been extensively revised and brought up to date. The general arrangement and format used in previous editions have been retained; however, there has been considerable rearrangement and improvement in the order of presentation of the material. Many chapters have been revised or completely rewritten in order to incorporate new knowledge and yet keep the volume within reasonable limits as to size.

In addition to presenting complete descriptive coverage of the animal parasites of man, the text emphasizes diagnosis, treatment, and partic-

ularly control measures of parasitic infections. It has been in this direction that workers in the field have been most interested for many years and with accumulated knowledge eradication of many diseases may be expected. Properly there is extensive treatment of these matters in this book. Any text of parasitology depends for effectiveness, of course, on illustrations. The present volume is exceptionally well illustrated by the judicious use of diagrams, drawings and photographs. Malarial parasites are shown in color.

The book is well bound, printed on good paper in easily read type. No typographic errors were noted. References are numerous and well chosen; the placing of them at the end of each chapter and subdivided as to subject is a valuable improvement over the previous listing in a separate section at the end of the volume. The index is divided into two parts, by author and subject; each is complete and permits easy location of material in the text. The book is highly recommended for everyone interested in any phase of parasitology. Every laboratory examining specimens for parasites should have a copy for reference and study. —*HOWARD A. VAN AUKEN, Col., MC, USA*

DE MOTU CORDIS (Movement of the HEART AND BLOOD in Animals). An Anatomical Essay by *William Harvey*. Translated from the original Latin by *Kenneth J. Franklin* and now published for the Royal College of Physicians of London. 209 pages; illustrated. Charles C Thomas, Publisher, Springfield, Ill., 1957. Price $3.50.

More than 300 years ago Sir Thomas Browne said of Harvey's discovery of the circulation of the blood: "Which discovery I prefer to that of Columbus." While we in America might differ from Sir Thomas on the relative merits of the two events it would seem that he divined the importance of Harvey's work. The well-known medical historian and bibliographer, Dr. John F. Fulton, made the original suggestion for a new translation of *De Motu Cordis* and it was done at the request of the Royal College of Physicians. It was felt that none of the previous versions were sufficiently accurate for those doing research either in the history or physiology of the circulation.

The first half of the volume is taken up by Dr. Franklin's translation; the remainder contains the Latin text of the 1766 edition. For readers with even "small Latin and less Greek" this gives an opportunity to compare the original with the English version. There are no notes and the only comments are to be found in the brief but illuminating preface and introduction. As an example, the translator makes it clear that to Harvey the heart meant the ventricles only and the auricles were considered as outside the heart. The reading of this classic of medicine by any physician is an interesting and stimulating experience. There is a fine colored reproduction of a famous protrait of Harvey as well as the four black-and-white figures of the original *De Motu Cordis*.

—*LOUIS H. RODDIS, Capt., MC, USN (Ret.)*

MEDICAL RADIATION BIOLOGY, by *Friedrich Ellinger,* M. D. 945 pages; illustrated. Charles C Thomas, Publisher, Springfield, Ill., 1957. Price $20.

This work covers in a single volume the medical aspects of ionizing radiation, ultraviolet, and visible light. For one person to attempt to write a comprehensive treatise in medical radiation biology is indeed an ambitious task. Radiation biology is a broad scientific discipline, heavily dependent upon physics and chemistry and encompassing within biology many subspecialties. Restriction to medical radiation biology eliminates from consideration only a part of the biology involved; all or almost all the physics and chemistry remains. It is inevitable that in a field so heavily dependent upon a number of scientific disciplines and their subspecialties and interrelationships that a work by a single author must suffer from the inability of a reviewer to analyze critically, let alone keep abreast of the rapidly increasing knowledge in this field.

This book contains much information not previously brought together. Ionizing radiation is discussed extensively, largely a result of both current and past interest. Missing from the section on ionizing radiation was a discussion of RBE (relative biological effectiveness). While there are many difficulties, practical and theoretical, the concepts and results involved in the determination of RBE do serve a useful purpose, particularly in health physics. The bibliography is very extensive, with a good representation of both the older and the European literature. While the table of contents is complete, this is not an adequate substitute for an index, the omission of which decreases the value of this book as a reference work. The book is of greatest value to those who desire a broad review with sufficient detail.

—*NATHANIEL I. BERLIN, Lt. Comdr., MC, USNR*

ANESTHESIA, A Manual for Students and Physicians, by *Stuart C. Cullen,* M. D. 5th edition. 295 pages; illustrated. The Year Book Publishers, Inc., Chicago, Ill., 1957. Price $5.50

This is the fifth edition of a manual which was first published in 1946. It is not a complete text in anesthesiology, but a teaching manual for medical students, part-time anesthetists, and physicians who may be called upon to care for respiratory emergencies, hypoxia, and shock. The author makes no attempt to include specific technical details. Emphasis is placed on establishing a basis for a rational approach to the solution of problems in anesthesia.

In this edition there is an entire revision of the chapter on use of depressant drugs. The emphasis has been shifted from a consideration of drugs to a consideration of the patient and his needs. The author has eliminated the comprehensive table of drug dosages for preanesthetic medication, which appeared in the fourth edition, because of his belief that additional experience in the use of depressant drugs makes one less inclined to defend the presentation of fixed patterns

in doses and combinations of depressant drugs. A section on cardiac arrest and its management has been added to the chapter on ventilation. The section on muscle relaxants in the chapter on inhalation anesthesia has been revised. Much has been written condemning the manner in which relaxant drugs are used. Information is given that is essential to safe and skillful use of these drugs. Minor additions and deletions have been made in a table of drugs commonly used for nerve blocks and spinal analgesia.

This manual provides an excellent source of information on the basic practice of anesthesia and is highly recommended for medical students and physicians who are interested in anesthesia.

—*JAMES G. KURFEES, Capt., MC, USN*

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, Volume 68, Art. 1, pages 1-244, August 30, 1957, editor-in-chief, *Otto V. St. Whitelock.* "Proteolytic Enzymes and Their Clinical Application." Consulting Editor and Conference Chairman: *Gustav J. Martin.* 244 pages; illustrated. The New York Academy of Sciences, New York, N. Y., 1957. Price $3.50.

The 22 papers which compose this volume resulted from a conference bearing the same title, held by the Section of Biology of the New York Academy of Sciences, 8 and 9 November 1956. The purpose of the collected papers, to provide a broad coverage of current experimental and clinical studies on the proteolytic enzymes, is admirably achieved.

Part I, entitled *Laboratory Studies,* contains papers on the chemical purification and properties of proteolytic enzymes, the development of a concept of the blood fibrinolytic system in which proactivator and plasminogen are represented as a single substance, and the production of intra- and extravascular fibrolysis in experimental animals by the intravenous administration of streptokinase. Gordon and Ablondi summarize their findings relative to the instillation of mustard oil into the eye of the rabbit, wherein the prior intravenous administration of streptokinase decreased the severity of the resultant inflammation. A highly productive paper by Ambrus et al. is concerned with methods for the objective in vivo evaluation of fibrinolytic agents, and includes emergent findings relative to dose levels and the therapeutic value of plasmin administered to patients with thromboembolic complications.

Part II is devoted to a broad spectrum of *Clinical Studies.* Included are studies on the use of pancreatic dornase aerosols in bronchopulmonary disease, of pancreatic dornase, trypsin, and Varidase in veterinary medicine, and of Varidase and trypsin in surgical lesions. Other papers record a wealth of clinical experience in the intravenous use of plasmin and streptokinase, the use of proteolytic enzymes in neurosurgery, and in the treatment of chronic chest diseases, traumatic injuries, and thrombophlebitis. The last of these studies is particularly impressive because of its attainment of statistically significant conclusions relative to the trypsin therapy employed.

—*THADDEUS J. DOMANSKI, Col., USAF (MSC)*

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, Volume 69, Art. 1, pages 1-254, Sept. 7, 1957, editor-in-chief, *Otto V. St. Whitelock.* "Biological Applications of Infrared Spectroscopy." Conference Co-Chairmen: *Robert P. Bauman* and *Carl Clark.* Consulting Editor: *Robert P. Bauman.* 253 pages; illustrated. The New York Academy of Sciences, New York, N. Y., 1957. Price $3.50.

This monograph, consisting of 15 excellent papers authored by 31 scientists and citing over four hundred references, resulted from a conference on the biological applications of infrared spectroscopy at the New York Academy of Sciences in December 1956. Often detailed, the subject matter assessed the contributions to infrared methods made by a variety of fractionation procedures, dealt with the interpretation of infrared intensity data as related to molecular composition, and discussed the influences of intra- and extramolecular structure on infrared phenomena attributable to certain functional groups including the more puzzling results obtained with some simple hydrogen-bonding systems. Also covered were studies of the solid-state infrared absorption of optically active, racemic, straight-chain α-amino acids, and investigations using lipids from serum and tissues and from different strains of mycobacteria. Exploratory infrared experiments using a variety of tissues, virus, and bacteriophage preparations were described, along with a microtechnic employing appropriate refinements of monochromator optical systems. The application of infrared spectroscopy in the pharmaceutical industry and adaptations of computer electronics to automatic analysis of infrared spectra were mentioned. A bibliography of infrared spectra of biochemicals was set forth. The monograph will be most appreciated by those well versed in infrared research, though the several technical papers will interest most workers busy with spectrometric problems, infrared and otherwise. Teachers and other researchers curious about recent scientific advances will find the papers readable and full of convincing examples of the avenues opened by infrared technology. However, they, along with those uninitiated in spectrometric methods, will have to refer to other sources for instrumentation information and the more elementary, fundamental data essential to appreciating what now in reality is a quite specialized facet of spectroscopy. —*CLAYTON S. WHITE, M. D.*

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, Volume 70, Art. 1, Pages 1-152, August 30, 1957, editor-in-chief, *Otto V. St. Whitelock.* "The Role of I^{131}-Labeled Proteins in Biology and Medicine." Conference Chairman and Consulting Editor: *S. P. Masouredis.* 152 pages; illustrated. The New York Academy of Sciences, New York, N. Y., 1957. Price $3.

This volume consists of 12 papers presented at a conference held by the Section of Biology of the New York Academy of Sciences in November 1956. They are generally divided into those relating to the methodology of labeling and various applications of the labeled proteins. Studies relating to antibody response, tissue localization and the dynamics of circulating summarize the current status of the art. Perhaps

the most valuable contribution of the volume relates to the problems associated with evaluating the biological aspects of labeled materials. With the addition of I^{131} the protein itself is obviously altered and, in a number of cases, the result is a change in the metabolic role of the protein. Further, the effect of the energies of the beta and gamma radiations of I^{131} must be considered because they are just within the range required to break certain chemical bonds. Finally, several functional discrepancies between compounds labeled with I^{131} and those with C^{14} or other isotopes are pointed out. The meaning of these discrepancies is still not clear. This volume should be read by all of those interested in research with tagged proteins or administering these compounds in clinical practice.—*JAMES B. HARTGERING, Lt. Col., MC, USA*

INTRODUCTION TO CLINICAL ENDOCRINOLOGY, by *A. Stuart Mason,* M. A., M. D. 192 pages. Charles C Thomas, Publisher, Springfield, Ill., 1957. Price $4.50.

This book does exactly what the author states is his intention in the preface, that is to present an introduction to clinical endocrinology. He does this by presenting information about the physiology of the individual ductless glands, its relationship to other glands, the diseases caused by dysfunction, a description of the definite clinical symptoms, steps in diagnosis, and available treatment. All this is presented in a didactic manner, putting forth accepted information in a logical, concise style which is intended to give the medical student a total view before he takes off into the obscure byways. The book is readable and contains many pertinent observations. Although intended primarily for medical students, anyone can benefit from its logical, brief review.

The short first chapter on the physiology of endocrine glands is especially good. The control of bodily functions by hormones and the effect of general medical disorders on the endocrine glands must both be considered, the author brings out. He devotes considerable space to thyroid and adrenal glands but this seems justified because thyroid disorders are the most common endocrine conditions and the most readily treatable. The adrenal is of great interest because of the recent work on the steroids. The appendix gives a sensible appraisal of a test of endocrine function.—*JAMES L. TOBIN, Col., USAF (MC)*

DISEASES OF THE EXTERNAL EAR, by *Ben H. Senturia,* A. B., M. D. American Lecture Series, Publication No. 319, A Monograph in The Bannerstone Division of American Lectures in Otolaryngology, edited by *Norton Canfield,* M. D. 211 pages; illustrated. Charles C Thomas, Publisher, Springfield, Ill., 1957. Price $8.50.

External ear infections are significant in the production of morbidity in personnel of the Armed Forces. These patients are difficult to treat. Therapeutic regimens to date have not been wholly satisfactory, and recurrences of infection are very common. Because there was no clear-cut understanding of the fundamental nature of these diseases, the Medical Service of the United States Air Force supported in part the investigation of this problem. This monograph is a culmination of this work.

The first portions of the book contain reviews of the literature of the factors presumed to be responsible for external ear infections, a classification of the various diseases, a review of the microbiological findings, and histologic studies of normal and diseased ear canal skin. Next, the experimental studies evolved to test this information, both animal and human, are described. The painstaking microchemical procedures that led to the development of artificial ears, the elaboration of therapeutic principles, and the extensive field trials of both prophylactic and curative regimens are recounted. The results of these trials are analyzed and a logical system of therapy is presented.

Because of personal experience with this work as an Armed Forces' project, this reviewer is familiar with the experimental design established and the results analyzed. For the otologist and the dermatologist this volume will serve as an excellent and fascinating guide through the maze of diseases of the external ear. The general practitioner will find the chapter on treatment a classic of both principles and specific therapy.—*JAMES E. LETT, Lt. Col., USAF (MC)*

THE MALABSORPTION SYNDROME, A Mount Sinai Hospital Monograph. Editor: *David Adlersberg,* M. D. Contributions to the Symposium by Members of the Staff of the Mount Sinai Hospital, New York. 252 pages; illustrated. Grune & Stratton, Inc., New York, N. Y., 1957. Price $5.50.

The subject of intestinal malabsorption is discussed in detail in this monograph. The book is comprised of a series of papers devoted to various aspects of the disorder. Because the authors are, for the most part, staff members of Mt. Sinai Hospital, they have had the opportunity to share in the detailed study and long-range observation of a large group of patients.

It is appropriate that the first paper should deal with physiology of intestinal absorption; the subject is covered in considerable detail and is augmented by an extensive bibliography. Following are a series of papers considering special aspects of the malabsorption syndrome, including those related to various metabolic disturbances, diagnostic technics and pathologic findings. Of particular interest are the presentations devoted to clinical aspects and management. It should be noted that idiopathic sprue, both tropical and nontropical, along with celiac disease, is considered as variations of the same basic disease. The similarities between these disorders, as well as the differences, are discussed in a very lucid manner. In regard to management, the authors present a relatively optimistic assessment of the therapeutic modalities presently available. For patients responding only indifferently to conventional dietary and supplement regimens, the use of long-term steroid therapy has often been quite successful in their experience. The monograph is of particular interest to gastroenterologists, but it is highly recommended to any physician whose sphere of interest includes this difficult medical problem.

—*HARVEY E. REITZ, Capt., MC, USN*

TECHNIQUE OF FLUID BALANCE, Principles and Management of Water and Electrolyte Therapy, by *Geoffrey H. Tovey*, M. D. 100 pages. Charles C Thomas, Publisher, Springfield, Ill., 1957. Price $2.50.

This small volume, almost handbook in size, is devoted to the important field of water and electrolyte therapy. The book is designed to furnish a succinct and practical outline of normal fluid balance and methods of correction of imbalance, the latter based on clinical appraisal when the physician does not have complete laboratory facilities available. The nine chapters are short and cover the normal composition of body fluids through the physiology of fluid balance to the consequences of depletion of the fluids and their components. Diagnosis and treatment of the various deficits are presented with some of the adverse effects of treatment. The final chapter discusses technics and includes some practical fluid balance charts. The appendices include units of measure, constituents of the various parenteral fluids, and laboratory methods for the physician who does not have available a flame photometer and other equipment found in the complete laboratory. The printing is excellent and the book is very adequately illustrated with understandable charts and diagrams. The few references at the end of the chapters are about equally divided between British and American publications. Interns and residents will find it appealing, as will the busy internist, surgeon, or pediatrician who deals with the problem in everyday practice. The author is to be commended for this publication. —*WILLIAM G. DUNNINGTON, Lt. Col., MC, USA*

IMPLANT DENTURES, Indications and Procedures, by *Aaron Gershkoff*, B. S., D. D. S., and *Norman I. Goldberg*, D. D. S. Foreword by *Irving R. Hardy*, D. M. D. 256 pages; 327 illustrations and 1 color plate. J. B. Lippincott Co., Philadelphia, Pa., 1957. Price $12.

This book is devoted to material concerned with implant denture construction, is indexed, and contains related bibliographies of appropriate material at the end of each chapter. The text is well organized, concise, and easily understood. Although the technics are well presented, it is doubtful if a reader would find himself qualified to attempt the construction of an implant denture from the text alone. This reviewer believes that the importance of the usual steps in denture construction *e. g.*, accurate jaw relationship records, face bow transfers, and the development of harmonious occlusions, are not sufficiently stressed in this text. These basic procedures are as important for the success of implants as they are for conventional dentures. Because of the interest in this new approach to the solution of some of the most perplexing of prosthodontic problems, both by the laity and the profession, and because the dental profession needs to have a better understanding of the technics and concepts of implant denture construction, this book is recommended as an addition to all professional libraries.

—*EDWIN H. SMITH, Jr., Lt. Col., DC, USA*

often extends research into new fields. It is unrealistic to consider research as a series of closed compartments. There must be relationship and fluidity among all types, and provision should always be made for continuity and adjustment when further exploration is indicated.

Almost as a corollary, one might consider an axiom true throughout history that any discovery of worldwide importance often is arrived at spontaneously in several areas simultaneously. Such results can never long be kept secret in one group or area, and furthermore, the dispersion of this knowledge is in direct proportion to the number of people involved.

Frank B. Berry

FRANK B. BERRY, M. D.
Assistant Secretary of Defense
(Health and Medical)

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Foreword

The *United States Armed Forces Medical Journal* is the medium for disseminating information of administrative and professional interest to all medical personnel of the Department of Defense. The Assistant Secretary of Defense (Health and Medical) and the Surgeons General of the several services invite all medical officers, dental officers, Medical Service Corps officers, Nurse Corps officers, and officers of the Veterinary Corps of the Armed Forces, and the medical consultants of the Army, Navy, and Air Force to submit manuscripts for publication in this *Journal.*

FRANK B. BERRY, M. D.,
Assistant Secretary of Defense (Health and Medical).

MAJOR GENERAL SILAS B. HAYS,
Surgeon General, United States Army.

REAR ADMIRAL BARTHOLOMEW W. HOGAN,
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